DISSERTATION ON

STUDY OF LIPID PROFILE IN INTRACEREBRAL HAEMORRHAGE

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations

for the award of the degree of

M.D. IN GENERAL MEDICINE

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THANJAVUR - 613 004

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

APRIL -2015

CERTIFICATE

This is to certify that this dissertation entitled " **STUDY OF LIPID PROFILE IN INTRACEREBRAL HAEMORRHAGE**'' is the bonafide original work of **Dr.DEEPIKA.S** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu Dr.M.G.R. Medical University to be held in APRIL - 2015. The period of the study was from December 2013 to August 2014.

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INTRODUCTION

Stroke is a neurological emergency. Stroke means being suddenly struck. It is also sometimes referred to as brain attack[1]. Stroke is one of the most important non communicable diseases causing death. Stroke or Cerebro Vascular Accident (CVA) is "abrupt onset of a neurologic deficit that is attributable to a focal vascular cause" [2]. World Health Organization defines stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin".

The two major categories of stroke are ischemic stroke and haemorrhagic stroke. Intracerebral haemorrhage attributes to 10.7 % of stroke from all causes[3]. It is diagnosed by a CT scan of brain which is the most important tool in evaluation of a patient with stroke. Intracerebral haemorrhage (ICH) is a grave disease inspite of growing knowledge in medicine. The outcome of patients is based on the severity of bleeding[4]. Symptoms are produced by the blood which causes mass effect disrupting the neural tissues, from the direct toxic nature of blood or due to increase in intracranial tension[5,6]. The fatality rate of ICH is high. There are limited treatment options available. Hence prevention of ICH is the most prudent way to limit the disease burden. This warrants thorough knowledge about various risk factors that predispose to ICH.

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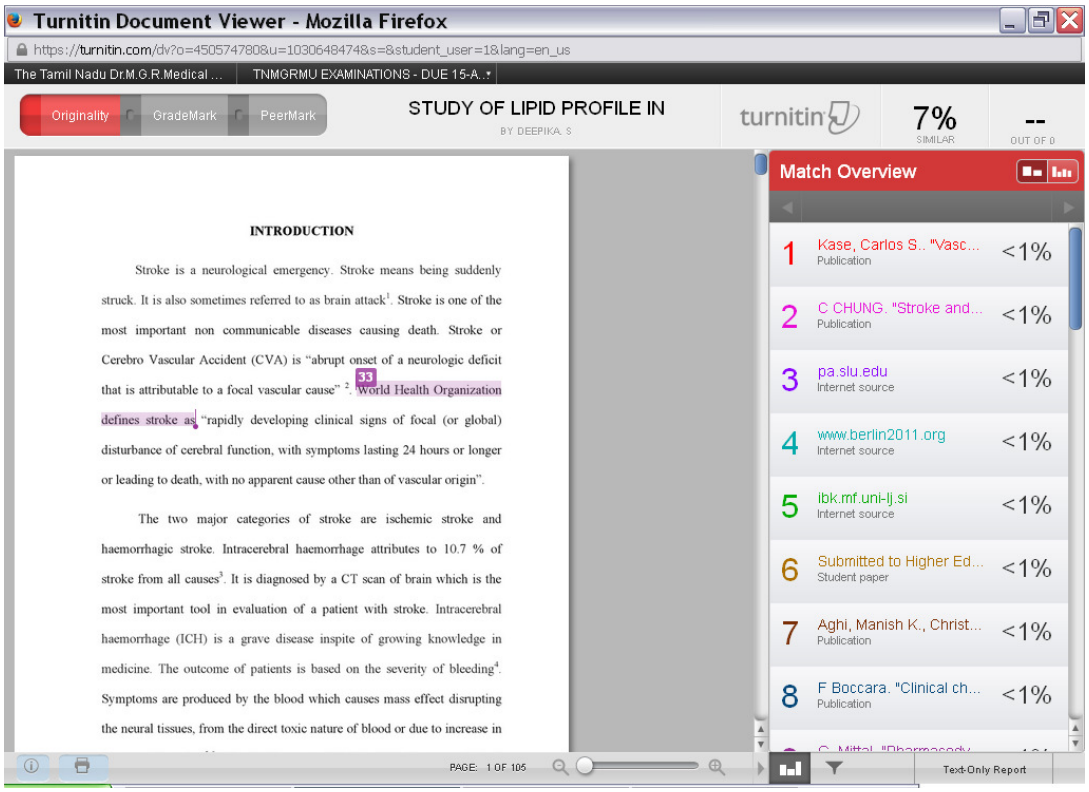
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LIST OF ABBREVIATIONS

CVA – Cerebro Vascular Accident

CT - Computed tomography

ICH- Intracerebral Haemorrhage

TC -Total Cholesterol

LDL-C -Low Density Cholesterol

HDL-C -High Density Cholesterol

VLDL-C- Very Low Density Cholesterol

TGL -Triglycerides

FDA-Food and Drugs Administration

MRI- Magnetic Resonance Imaging

CNS- Central Nervous System

HT- Hypertension

SHT- Systemic Hypertension

DM- Diabetes Mellitus

SAH- Subarachnoid Haemorrhage

AVM-Arterio Venous Malformations

CAA- Cerebral Amyloid Angiopathy

BP-Blood Pressure

ALL-Acute Lymphoblastic Leukemia

ICP- Intra Cranial Pressure

ICT- Intra Cranial Tension

MAP-Mean Arterial Pressure

IV- Intra Venous

FFP-Fresh frozen plasma

DVT-Deep Vein Thrombosis

FAST- Factor Seven for acute haemorrhagic Stroke Trial

LCAT- Lecithin Cholesterol Acyl Transferase

CETP-Cholesterol Ester Transfer Protein

CHOD-Cholesterol Oxidase

POD-Peroxidase

MRFIT- Multiple Risk Factor Intervention Trial

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ABSTRACT

STUDY OF LIPID PROFILE IN INTRACEREBRAL HAEMORRHAGE

BACKGROUND

Stroke caused by intracerebral haemorrhage (ICH) has high mortality rate. Among various risk factors for ICH, hypertension is the most important factor. Certain population studies have reported a paradox of inverse association between serum cholesterol and risk of ICH. This study is to look for correlation between lipid profile and ICH.

AIMS AND OBJECTIVES

The study is designed to evaluate the serum lipid profile

total cholesterol (TC), triglycerides (TGL), high density cholesterol (HDL-C),very low density cholesterol (VLDL-C) and low density cholesterol (LDL-C) in intracerebral haemorrhage patients and look for correlation.

METHODOLOGY

50 patients with ICH admitted in Thanjavur Medical College Hospital, Thanjavur who fulfilled the inclusion and exclusion criteria were selected. It is a hospital based observational study. History, clinical examination and investigations (CT & MRI Brain and basic blood biochemistry with serum lipid profile) were collected and the data were analysed statistically.

RESULTS

Majority of the ICH patients in our study were > 55 years and were males. Basal ganglia was the commonest site and hypertension was the important risk factor. The total serum cholesterol was < 200mg/dl in 72 % of our patients, with a mean of 168.09 ±43.74mg%. Serum triglyceride level was <150 mg/dl in 74%, with a mean of 124.12 ±50.76mg%. LDL-cholesterol was <130mg /dl in 68 % of patients, with mean of 108.26±43.31mg%. HDL-C was < 40 mg/dl in 76% of patients and VLDL-C was < 30mg/dl in 72% patients. The various lipid fractions observed were found to be low in majority of our ICH patients (p value < 0.05), suggesting a negative association between the two. The results obtained were comparable to other similar studies.

CONCLUSION

Majority of intracerebral haemorrhage patients in our study had lower levels of total cholesterol, triglyceride, HDL-C, LDL-C and VLDL-C. Whether the inverse association between serum lipid levels and ICH is a true causal association or only by chance due to other common confounding factors needs to be evaluated with large scale studies.

Key words: Intracerebral haemorrhage, lipid profile, serum cholesterol, triglyceride, HDL-C, LDL-C, VLDL-C.

INTRODUCTION

Stroke is a neurological emergency. Stroke means being suddenly struck. It is also sometimes referred to as brain attack[1]. Stroke is one of the most important non communicable diseases causing death. Stroke or Cerebro Vascular Accident (CVA) is "abrupt onset of a neurologic deficit that is attributable to a focal vascular cause" [2]. World Health Organization defines stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin".

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way to limit the disease burden. This warrants thorough knowledge about various risk factors that predispose to ICH.

Hypertension is the most important and well established risk factor for ICH[7,8]. Other risk factors are race, alcoholism, smoking, coagulopathy, thrombocytopenia[9] etc. Certain studies have reported a paradox of increased ICH incidence among people with low serum cholesterol. This study is to see the various derangements in the lipid profile of patients with ICH and look for correlation.

AIMS AND OBJECTIVES OF THE STUDY

1. The study is designed to evaluate the serum lipid profile –
    a. Total Cholesterol (TC),
    b. Triglycerides (TGL),
    c. High Density Cholesterol (HDL-C),
    d. Very Low Density Cholesterol (VLDL-C) and
    e. Low Density Cholesterol (LDL-C) in intracerebral haemorrhage (ICH) patients.

2. To assess for correlation between lipid profile levels and intracerebral haemorrhage (ICH).

REVIEW OF LITERATURE

HISTORICAL ASPECTS [10, 11]

Stroke was initially called as apoplexy during the period of Hippocrates. It was in the early 16th century the word stroke came into use in the English literature. It was Galen who thought that it was due to interruption of flow of some "Vital Spirit" to brain which was later on found to be blood. Slowly the term apoplexy disappeared and was replaced by cerebrovascular diseases.

It was Osler who mentioned about massaging the affected limbs to prevent contractures. In 1946, Kubik and Adams gave clinicopathological analysis of occlusion of the basilar artery. Miller Fisher in 1951 gave the clinical profile of patients who had internal carotid artery (ICA) occlusions in the neck.

Later on different diagnostic and therapeutic changes came into limelight. It was way up in 1950 Lawrence Craven described the effect of aspirin on clotting of blood. In 1960s the idea of use of aspirin in preventing clotting disorders emerged. Major risk factors for stroke were stratified in 1960s and this caused fall in mortality. With advent of CT scans in early 1970s clear distinction could be made between ischemic and haemorrhagic strokes[12].

In 1990s tissue plasminogen activator (t-PA) was approved by FDA for ischemic strokes. At present the treatment of stroke is brought about by stroke unit which provides comprehensive assessment of various risk factors and holistic treatment.

EPIDEMIOLOGY

Stroke or Cerebro Vascular Accident (CVA) is sudden onset of focal neurologic deficit, caused by vascular lesion. Stroke has emerged as one of the most important causes of death among non communicable diseases. Mortality from stroke is high especially in Asia. It is also the major cause of disability in adults. 30% of stroke survivors need assistance for day care activities, 20% of survivors need help for walking and 16% of survivors need hospital care.

India bears the double burden of both non communicable and communicable diseases. Of the non communicable diseases stroke contributes to majority of cases. Rate of incidence of stroke in many population based studies in India is estimated to be 119-145/1,00,000 [13]. Gone are the days when stroke was considered to be a disease of affluent people. In recent times, the incidence of stroke is increasing among people in rural areas and people of lower socioeconomic status, thereby increasing the burden of the disease.

Broadly stroke is classified[14] as

1. Ischemic stroke (80%)

2. Haemorrhagic stroke (20%)

Haemorrhagic stroke includes

Intracerebral Haemorrhage (ICH) and

Subarachnoid Haemorrhage (SAH)

10% of all strokes are due to ICH. The significance of ICH comes from the fact that 30 day fatality rate is as high as 50%.

Ischemic stroke[14]

Common etiologies of ischemic stroke are large vessel thrombosis, lacunar stroke, artery to artery embolus especially from carotids, cardioembolic causes like atrial fibrillation, myocardial infarction, valvular lesions and endocarditis.

Uncommon etiologies include hypercoagulable states, vasculitis, fibromuscular dysplasia and moyamoya disease.

INTRACEREBRAL OR INTRAPARENCHYMAL HAEMORRHAGE

HYPERTENSION

The single most important cause for ICH is hypertension[7, 8].

NON HYPERTENSIVE CAUSES [7]

- Vascular malformations like
    - arteriovenous malformations (AVM),
    - saccular aneurysms,

- cavernous angiomas

- Cerebral Amyloid Angiopathy (CAA)
- Tumors
- Bleeding disorders
- Use of anticoagulants
- Use of fibrinolytic agents
- Vasculitis
- Sympathomimetic agents (including amphetamine and cocaine)
- Haemorrhagic infarction
- Trauma
- Hemoperfusion Syndrome

PATHOGENESIS OF ICH [5, 15]

Presence of long standing systemic hypertension leads to fibrinoid necrosis of the penetrating and sub cortical arteries, thereby causing their walls to become weak. This leads to tiny outpouchings called Charcot-Bouchard micro-aneurysms, the main factor predisposing to ICH.

The main sources of bleeding are from the deep penetrating arteries of the circle of Willis, including the lenticulostriate, thalamogeniculate, thalamoperforating arteries and basilar artery perforators. Any abrupt raise in blood pressure also precipitates ICH. Rupture of vascular malformation is the next common cause for ICH.

If the blood volume is large it distorts the neural structures and raises intracranial tension causing midline shift sometimes leading to herniation and death.

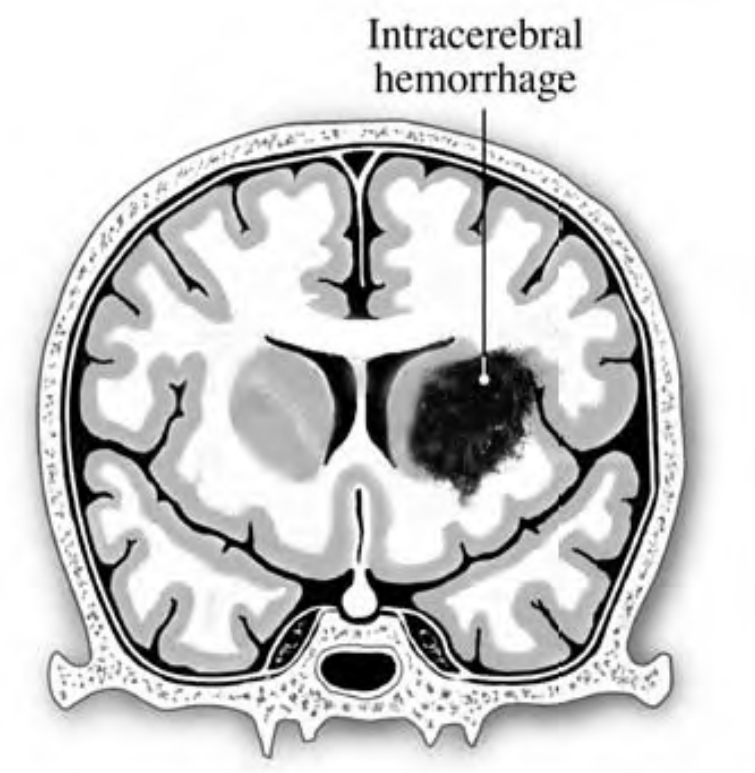


FIGURE.1. INTRACEREBRAL HAEMORRHAGE

CAUSES OF INTRACEREBRAL HAEMORRHAGE:

HYPERTENSION:

Systemic hypertension is the major cause for ICH. It accounts for about 72 % to 81% of ICH[16, 17]. The common sites of hypertensive ICH are putamen, cerebral lobes, thalamus, pons, caudate and cerebellum[4].

Hypertensive intracerebral haemorrhages are also called primary ICH and only around two percent of hypertensive ICH occur in multiple sites in brain. Primary intraventricular haemorrhage is uncommon. If it occurs it is probably due to bleeding from choroid plexus. Hypertension also adds to the risk of rupture of the arteriovenous malformations (AVM) and aneurysms.

NON HYPERTENSIVE CAUSES

VASCULAR MALFORMATIONS[18, 19, 20, 21]

Vascular malformations like arteriovenous malformations (AVM) or cavernous angiomas can cause ICH. These occur often involving the cerebral sub cortical white matter.

There are certain peculiarities among this subgroup of patients compared to hypertensive ICH.

- There size of haematoma with this type of ICH is smaller.
- The onset of clinical features is slower.
- If there is coexisting subarachnoid haemorrhage (SAH) in the imaging, it is a clue to etiology of vascular malformation.
- Younger individuals are affected by this type of ICH.
- The occurrence of such ICH is higher among females as opposed to hypertensive ICH.

AVM can occur in both brain and spinal cord. It has a tangle of blood vessels which has a number of feeding arteries with one large vein that drains it without capillaries connecting these two.

Any abrupt increase in blood pressure or trivial trauma can cause haemorrhage. These are frequently lobar haemorrhages as opposed to hypertensive bleeds that occur in basal ganglia.

Cavernous angiomas are frequently supratentorial involving frontal, temporal and parietal lobes. These are mostly asymptomatic but can cause ICH. The tendency to bleed is comparatively lesser with cavernous angiomas as opposed to AVM. They rarely present as progressive deficits due to recurrent and small bleeds. In MRI Brain, cavernous angiomas are seen as irregular lesions with mixed T2 signal in centre and low intensity signal surrounding it. Saccular aneurysms that are usually associated with SAH can also cause ICH. Charcot Bouchard aneurysms are small outpouchings of perforating arteries which represent a degenerative process as a result of chronic hypertension and are hypothesized to be associated with ICH[22, 23].

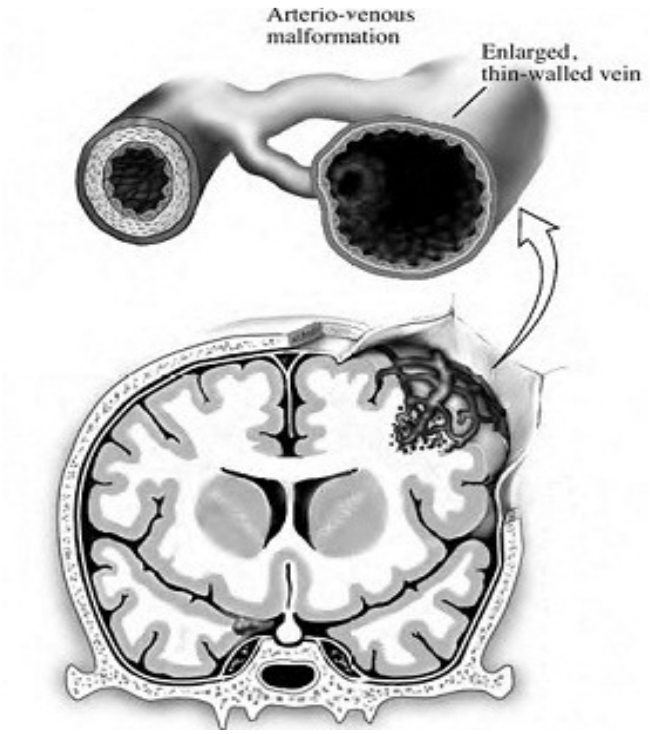


FIGURE 2.ARTERIOVENOUS MALFORMATION

CEREBRAL AMYLOID ANGIOPATHY (CAA)

Deposition of Congo red positive amyloid in the cerebral blood vessels most often the small and medium sized ones are characteristic feature of cerebral amyloid angiopathy[24].There is breakdown of the blood vessel wall. The amyloid that is associated with CAA is Aβ type. This process mainly affects the blood vessels of cerebral cortex and the leptomeninges. The process affects patchy areas of brain alternating with normal areas. Severe cases will have development of micro aneurysms, vessel wall splitting, vessel wall inflammation or fibrinoid necrosis.

The incidence of CAA rises with increasing age[25]. Almost 60% of autopsies in elderly over 90 years of age have revealed this pathological change[26]. The presence of amyloid weakens the vessel wall and leads to rupture of the blood vessel. CAA causing ICH is rare among younger individuals less than 55 years of age.

ICH associated with CAA is frequently lobar owing to the fact that the affected vessels are superficially located. The disease process affects blood vessels widespread in the brain so they are common causes of multiple and recurrent ICH in older population. Similar pathological process occurs in individuals with Alzheimer's disease[27]. CAA is associated with certain cases of dementia, seizures or TIA.

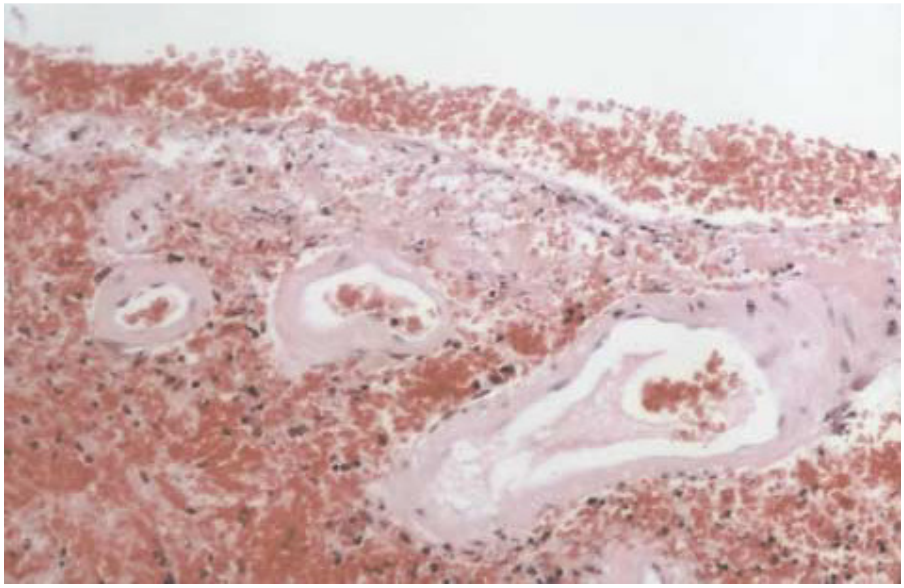


FIGURE 3. AMYLOID ANGIOPATHY SHOWING AMYLOID DEPOSITS IN THE VESSEL WALL

TUMORS

The occurrence of ICH as a result of brain tumor bleed accounts only for a rare subset of patients around 10% of ICH [28,29]. This can occur both with primary or metastatic malignancies. The most common tumors associated with ICH are metastatic malignant melanoma, choriocarcinoma, renal cell carcinoma, primary brain tumors like glioblastoma multiforme and oligodendroglioma[28,30,31] . The propensity of the tumor to bleed depends upon the vascularity of the tumor and the malignant nature of the tumor. There is additional component of vessel wall invasion for metastatic choriocarcinoma. ICH may be the first manifestation of the tumor in certain cases.

Imaging and clinical features suggestive of tumor bleed[33, 34] are

- Papilledema during presentation.
- Unusual site of occurrence of bleed as compared to hypertensive ICH.
- Multiple haemorrhages.
- Haematoma being spherical.
- Non contrast CT Brain shows a low density central area due to necrosis surrounded by high density ring.
- Gross cerebral edema out of proportion to the amount of bleed.
- Presence of contrast enhancing lesion in the surrounding.

Tumor bleeds carry grave prognosis with high mortality rate.

BLEEDING DISORDERS

Coagulation disorders are rare causes of ICH. Hemophilia causes ICH in 2.5-6 % of affected patients. ICH is an important complication of acute leukemias particularly ALL. Thrombocytopenia especially when platelet count falls less than 10,000 causes ICH.

USE OF ANTICOAGULANTS

Use of anticoagulants has been associated with increased incidence of ICH about 8 to 11 times that of normal population. About 10% of cases of ICH are due to use of anticoagulants[34,35].Greater the degree of anticoagulation, higher is the risk particularly when the International Normalised Ratio (INR) >4 [37,38]. This type of ICH has peculiar feature that it occurs over a protracted period. Cerebellar and lobar ICH have this type of ICH as a common cause next to hypertension. The mortality rate is higher with this type and there is also greater tendency for the haematoma volume to expand. Leukoaraiosis when present in large areas has a greater risk of bleed with concomitant anticoagulant use.

FIBRINOLYTICS

ICH is a serious complication with use of fibrinolytics like streptokinase and tissue-type plasminogen activator (t-PA). This complication frequently follows shortly after thrombolysis. Usually the site of bleed in such cases is lobar. ICH occurs as a complication of use of recombinant t-PA (rt-PA) used for intravenous thrombolysis for acute

ischemic stroke. The incidence of ICH in intravenous thrombolysis for acute ischemic stroke is about 6.4%. Intra arterial thrombolysis also causes ICH in about 11% of cases[38,39].

Risk factors for this complication are large stroke with major neurological deficit during treatment, mass effect and edema in CT Brain, presence of hyperglycemia and longer duration between onset of stroke and initiation of thrombolytic therapy[40].

VASCULITIS

Cerebral vasculitic disorders usually cause ischemic stroke. The rare cause of ICH among the vasculitic disorders is Granulomatous angiitis of the CNS otherwise called as isolated angiitis of CNS[41].

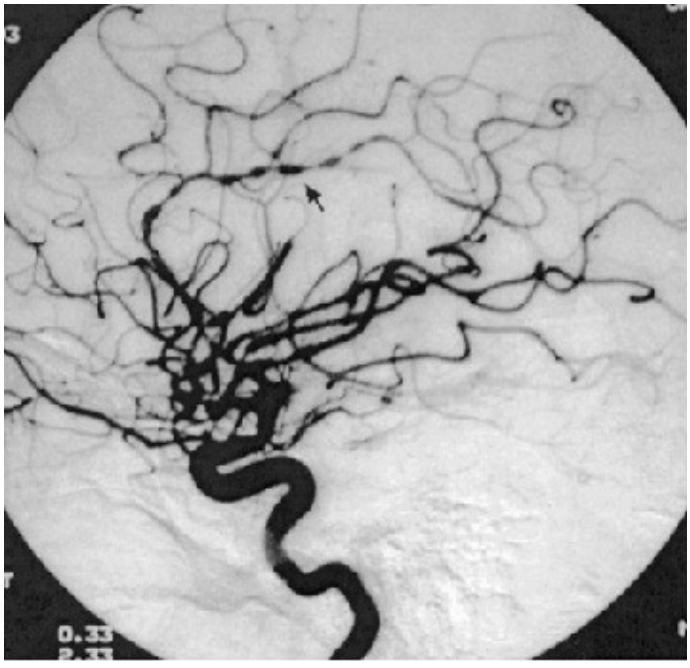


FIGURE.4 BEADING OF VESSELS IN ANGIOGRAPH OF ISOLATED ANGIITIS OF CNS

Isolated angiitis of CNS occurs without any features of systemic disease like fever, weight loss or elevated erythrocyte sedimentation rate (ESR)[42]. There is infiltration of mononuclear cells in the walls of cerebral arteries and veins. It may also be accompanied by micro aneurysms. The site of bleed is usually lobar. The CSF shows lymphocytic pleocytosis with increase in protein. Angiography reveals beading of the affected blood vessels.

Polyarteritis nodosa may also cause ICH and it is usually associated with systemic features of vasculitis.

SYMPATHOMIMETIC DRUGS

The most common culprit drugs are amphetamine, methamphetamine and pseudoephedrine. All routes including intravenous, intranasal and oral abuse have been implicated. ICH occurs within minutes to hours after the drug has been taken. The site of bleed is usually sub cortical white matter. The main mechanisms predisposing to ICH are due to transient increase in blood pressure and also due to spasm of blood vessels in response to the drug[44]. Sometimes there is associated beading of the blood vessels but it is reversible with treatment of steroids.

Phenylpropanolamine, a nasal decongestant and anorexigenic drug is also implicated as a cause of ICH. Cocaine causes both ICH and SAH. ICH is usually in the sub cortical white matter. It is mainly due to drug induced vasoconstriction and vasculitis.

HAEMORRHAGIC INFARCTION

Haemorrhagic transformation of the infarction is a dreadful complication. Scattered petechial haemorrhages are seen in the necrotic tissue. Main risk factors are large infarcted tissue, embolic stroke and cerebral venous sinus thrombosis. It occurs due to reperfusion of the damaged blood vessels in the necrotic area.

The distinguishing features of haemorrhagic infarction from that of primary ICH are

- Usually associated with an embolic source.
- Features of raised ICT are absent.
- CT Brain shows spotted areas of hyperdensity without midline shift.
- Usually cortical in location.
- Ventricular bleed is uncommon.
- Branch occlusion in angiography.

HEAD TRAUMA

Intracranial haemorrhages may be caused by cerebral contusion injury. It is classified under traumatic bleed. Usually they are multiple and occur in basal frontal, anterior temporal and occipital areas.

HEMOPERFUSION SYNDROME

This is a rare cause of ICH occurring in about 1% of cases after carotid endarterectomy especially in the initial postoperative period. It occurs mostly in those patients where there is hemodynamically compromised cerebral circulation prior to the procedure. It may also occur after carotid stenting.

RISK FACTORS FOR ICH[9]

AGE

Increasing age is an important factor predisposing to ICH.

RACE

Certain groups of population have an increased risk of developing ICH like the Africans, Asians and Hispanics.

SYSTEMIC HYPERTENSION

Systemic hypertension is the most important and most well studied risk factor for ICH.

ALCOHOL[45,46]

Consumption of alcohol especially in large amounts [more than 21 units per week] is a risk factor.

SMOKING[47]

Smoking is associated with risk of ICH, especially in those who smoke more than 20 cigarettes a day.

LOW CHOLESTEROL[48,49]

There are many population based studies that have revealed that low serum cholesterol levels [especially when less than 160mg %] are associated with sizable increase in the occurrence of ICH.

GENETIC FACTORS[50]

Presence of certain alleles of apoE $\in 2$ and $\in 4$ are associated with more risk of ICH due to cerebral amyloid angiopathy.

CLINICAL FEATURES[51,52]

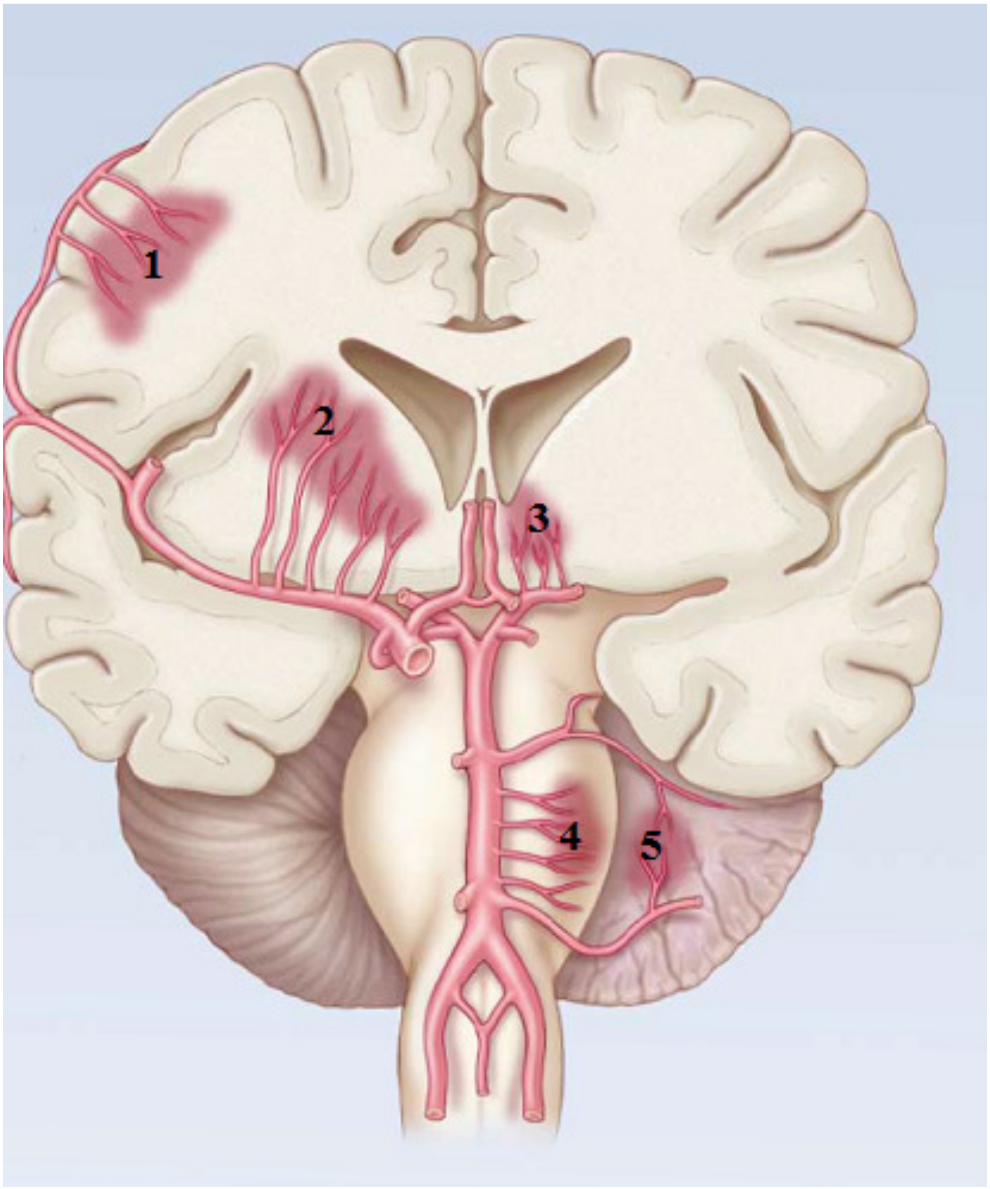
In the pre CT scan era the distinction between a haemorrhagic stroke and ischemic stroke was mainly relied upon on the mode of onset and the characteristic clinical features. Depending on the amount of blood and the site of bleed there are different clinical presentations.

ICH usually occurs while the patient is awake and during activity in contrast to ischemic stroke where the patient wakes up with neurological deficit. The features of increased intracranial tension like headache[53], vomiting and altered consciousness are present. Altered sensorium is present in about 60% of patients with more than half worsening to the level of coma. Coma occurs mainly in those with intraventricular extension. The presence of coma in a case of ICH also signifies that it is massive and is usually associated with grave prognosis. Patients with SAH may also have additional features of neck stiffness and features of meningism.

The neurological deficit in ICH often shows progression over period of hours relating to progressive increase in the haematoma volume. The amount of neurological deficit also depends upon the site of haemorrhage. Seizures occur only in a small subset of patients especially more common in those with lobar haemorrhage.

Hypertension is common at the time of presentation. Patient also will have other features of hypertension like left ventricular hypertrophy, hypertensive retinopathy and nephropathy. Unlike non hypertensive causes of ICH that tend to evolve slowly, hypertensive ICH usually evolves within short period of around 30–90 minutes.

The various topographical locations of ICH present with different neurological findings[4]. The site of ICH also depends upon various etiologies and therefore can be a clue towards etiological diagnosis. Hypertensive haemorrhages most commonly involve basal ganglia. Lobar haemorrhages can be due to hypertension in 50% of cases but can also be associated with many non hypertensive causes.



1. cerebral lobes;2.basal ganglia; 3.thalamus; 4.pons; 5.cerebellum

FIGURE.5.COMMON SITES OF ICH

PUTAMINAL HAEMORRHAGE

Putamen is the most common site of ICH, accounting for about 35% of ICH. It is commonly associated with internal capsule involvement. It is classically associated with contralateral motor weakness, sensory

disturbance, aphasia and sometimes visual disturbances. Homonymous hemianopia and horizontal gaze palsy can occur.

If the bleed is massive, it can cause coma and uncal herniation. Uncal herniation causes third nerve palsy and presents with pupillary abnormality. The presence of third nerve dysfunction is one of the poor prognostic signs. The presence of intraventricular extension of the ICH is also a poor prognostic factor.

CAUDATE HAEMORRHAGE[54]

It occurs in about 5% of patients of ICH. The most common etiology is hypertension. The source of bleed is the penetrating arteries of anterior and middle cerebral arteries. The onset of the disease is abrupt with headache and vomiting.

There is frequent intraventricular extension leading to hydrocephalus. Usually there are neuropsychological abnormalities like abulia, disorientation and amnesia. Motor weakness is usually mild. There is no aphasia. Caudate haemorrhages have a benign course and good outcome. Patients usually recover fully without any neurological deficit. But some may have persistent neuropsychological abnormalities.

THALAMIC HAEMORRHAGE

10 to 15% of ICH is due to thalamic haemorrhages. The most common cause is hypertension. Depending on the size of haematoma, it can enlarge medially to the third ventricle, laterally into the internal capsule,

superiorly into the parietal white matter and inferiorly into dorsal midbrain and sub thalamic nuclei. There is abrupt onset of contralateral motor deficit with hemi sensory loss.

The most important oculomotor findings are vertical gaze palsy, miotic and unreactive pupil. These patients sometimes have Parinaud syndrome. Large haematoma volume and presence of hydrocephalus are poor prognostic signs.

LOBAR HAEMORRHAGE

Lobar haemorrhage is the second most common cause of ICH contributing to about 25% of cases. These are the sub cortical white matter haemorrhages. Any cerebral lobe can be affected but involves most commonly the parietal, temporal and occipital lobes.

Hypertension is the cause in about 50% of cases. The peculiarity of lobar haemorrhages is that there are non hypertensive causes related to lobar ICH like AVM, intracranial tumors, use of sympathomimetic drugs, bleeding disorders and in the elderly cerebral amyloid angiopathy. Lobar haemorrhages present with headache, seizures, sensorimotor deficits and aphasia. The occurrence of coma is less frequent. Death from lobar ICH is usually lower than that from other sites of ICH.

CEREBELLAR HAEMORRHAGE

5 to 10% of ICH are due to cerebellar haemorrhage. These originate from superior cerebellar or posterior inferior cerebellar arteries.

Hypertension is the common risk factor for cerebellar ICH. Few cases have been associated with rupture of AVM and anticoagulant use.

The patient typically presents with sudden onset of vertigo, inability to stand and gaze palsy. Headache and vomiting are more common with cerebellar ICH. There is ipsilateral appendicular ataxia and ipsilateral gaze palsy. The course of cerebellar ICH is often not predictable. Features of increased ICT and brainstem compression are more common complications of cerebellar ICH. Brainstem compression is frequently the cause of mortality. Such patients need urgent surgical decompression, which improves outcome.

PONTINE HAEMORRHAGE[55]

5% of cases of ICH are due to pontine haemorrhages. Pontine haemorrhages occur bilaterally and are usually due to hypertension. There is frequent extension of this type of ICH into the fourth ventricle. Severe headache occurs and the patient rapidly deteriorates to coma. Quadriplegia with spasmodic decerebrate posturing and hyperthermia with pinpoint pupils occur. There is also horizontal gaze palsy with one and a half syndrome and ocular bobbing.

Massive haemorrhage can lead to death within few hours. Hyperthermia, tachycardia, respiratory abnormalities and hydrocephalus are predictors of mortality.

MESENCEPHALIC HAEMORRHAGE

Mesencephalic haemorrhages are rare. Usually it is an extension from thalamus, putamen, cerebellum or pons. Hypertension, rupture of AVM and blood dyscrasias are the causes. They present with ataxia, oculomotor palsy, vertical gaze palsy and contralateral hemiparesis. Midbrain ICH when small can solely present with isolated ophthalmoplegia.

MEDULLARY HAEMORRHAGE

Haemorrhage into medulla oblongata occurring in isolation is very rare. Usually it is an extension from pontine haemorrhage. Patients present with sudden onset of headache, dizziness, dysphagia, dysphonia, dysarthria, ataxia, nystagmus, Horner's syndrome, hiccups, limb weakness or hypoglossal nerve palsy. Hypertension, AVM and anticoagulant usage are common causes of medullary haemorrhage. Mortality rate is around 20%.

INTRAVENTRICULAR HAEMORRHAGE

Intraventricular extension of haemorrhage from caudate, thalamus, putamen and cerebral lobes is an important complication. Primary intraventricular haemorrhage is rare. It contributes to about 3 % of cases. The source of bleed for primary intraventricular haemorrhage is from the subependymal blood vessels. Hypertension, AVM, sympathomimetic drugs, tumors and blood dyscrasias are the causes. The patients typically present with sudden onset of headache, vomiting, altered sensorium and minimal neurological deficit. Among the cases having AVM those with anterior

communicating artery aneurysm usually rupture into the lateral ventricles. Small AVM that are situated in the medial part of thalamus and basal ganglia cause primary intraventricular haemorrhage. Sometimes AVM are located within the ventricles.

MRI Brain with angiography is more reliable in diagnosing the presence of AVM in such cases. Those patients who are alert initially recover with residual deficit. But those who are comatose initially have high degree of mortality due to brainstem compression.

DIAGNOSIS OF INTRACEREBRAL HAEMORRHAGE

CT BRAIN[32,56]

Sudden onset of symptoms with altered sensorium in a patient presenting with high blood pressure suggests a possible diagnosis of ICH.

The introduction of CT scan in 1973 by Hounsfield revolutionized the diagnosis of stroke patients, distinguishing the ischemic and haemorrhagic strokes. Non Contrast CT scan of the brain is the most sensitive and gold standard diagnostic tool to diagnose acute ICH. It is also less time consuming compared to MRI scanning.

Blood appears as hyperdense lesion in non-contrast CT brain. It appears dense and homogenous. There is associated mass effect. It remains hyperdense for few weeks and later on becomes isodense with surrounding brain tissue. The site of bleed, size, any intraventricular extension, mass

effect and presence of hydrocephalus can be found by CT Brain. Late contrast enhancement in CT Brain may occur after 2 to 4 weeks and can remain so for long time in few cases.

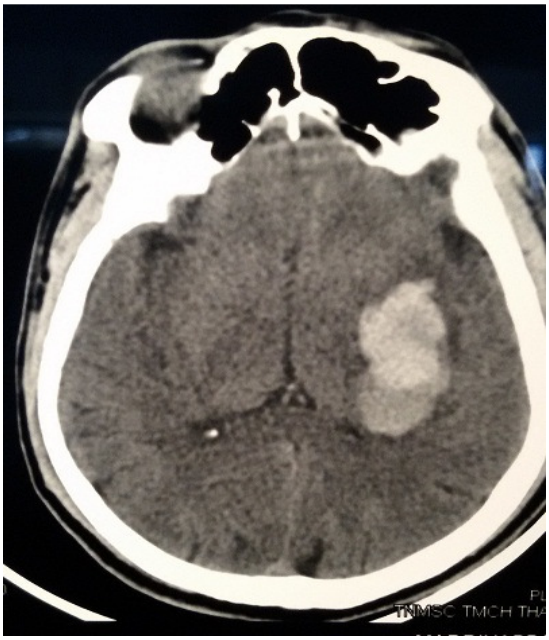


FIGURE 6. NON CONTRAST CT BRAIN SHOWING ACUTE LEFT BASAL GANGLIA ICH

CT is more sensitive for supratentorial haemorrhages. As bone induced artifacts obscure clear viewing of posterior cranial fossa, CT scan is less reliable for posterior cranial fossa ICH. MRI is useful in posterior cranial fossa lesions.

Sometimes CT angiography is used in young patients to identify AVM. The presence of “dot sign” in post contrast CT is a sign that there is an active bleeding.

MRI BRAIN

DURATION AFTER ICH	SOURCE OF RADIOLOGICAL SIGNAL	T1-WEIGHTED MRI	T2-WEIGHTED MRI
Hyperacute (initial hours)	Oxyhaemoglobin	↔ Or ↓	↑
Acute (1–3 days)	Deoxyhaemoglobin	↔ Or ↓	↓↓
Early subacute (3–7 days)	Intracellular methaemoglobin	↑	↓
Late subacute (1–4 weeks)	Extracellular methaemoglobin	↑↑	↑↑
Chronic	Haemosiderin	↓	↓↓

TABLE.1. MRI BRAIN IN INTRACEREBRAL HAEMORRHAGE

↔ Isointense with surrounding brain

↓ Hypointense

↑ Hyperintense

↓↓ Marked Hypointense

↑↑ Marked Hyperintense

Interpretation of ICH in MRI is more complicated. There is a change in appearance of haemorrhage as the time advances because the red cells are lysed and there is degradation of hemoglobin that is engulfed by macrophages to form hemosiderin. Other factors like the amount of protein, water, fibrin and clot retraction also change the MRI appearance. Gradient echo (GRE) MRI or T2 susceptibility weighted MRI is important in diagnosis.

But the haemorrhage can mask the underlying cause in some cases. So in suspected patients a repeat MRI after 3 months has to be done to find the presence of underlying cause. Sometimes angiographic studies are needed. MRI is sensitive in diagnosing small ICH.

The presence of any cause for ICH can be delineated by MRI.

- AVM are seen as clusters of blood vessels.
- Cavernous angiomas are seen as small hyperintense lesions surrounded by hypointense rim.
- Tumor bleed is seen as a central hypointense lesion due to necrosis surrounded by hyperintense signal.
- Vasculitis may be suspected when there are coexisting ischemic and haemorrhagic lesions.

ANGIOGRAPHY

In order to find a potentially treatable cause for ICH, angiographic studies need to be done in selected patients. Angiography is indicated in any young patient with ICH and certain elderly patients with lobar haemorrhage.

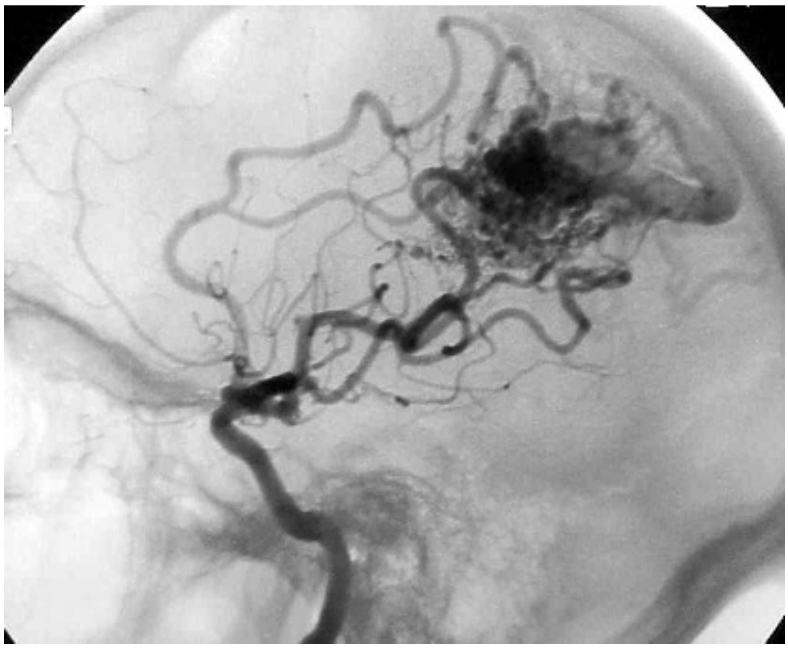


FIGURE.7.ANGIOGRAPHIC PICTURE SHOWING ARTERIOVENOUS MALFORMATION

The presence of aneurysms, AVM,cavernous angiomas or CNS vasculitis can be identified by angiography.

In a study Zhu et al, the angiographic abnormalities were found in 48% of cases less than 45 years of age as opposed to 0 to 10% of older

patients. If the initial angiography is negative, it may be repeated 2 to 4 weeks after the haematoma resolves in those patients where secondary causes of ICH are strongly suspected.

HAEMORRHAGES IN MULTIPLE SITES

Presence of multiple haemorrhages in neuroimaging may suggest

- Cerebral amyloid angiopathy
- Tumor bleed
- Bleeding disorders
- Use of thrombolytics
- Cerebral vasculitis.

MANAGEMENT

INITIAL EVALUATION

Intracerebral haemorrhage is a medical emergency. The comprehensive and coordinated work of critical care physician, neurologist, radiologist and neurosurgeon is of utmost importance. Most of the patients are comatose while they arrive at the casualty.

- The first 24 hours is the most crucial part of management. The American Stroke Association advises Intensive Care management especially during this period.
- Airway, Breathing and Circulation should be maintained.
- Early endotracheal intubation should be done in comatose individuals to protect the airways, to prevent aspiration and hypoxia.

- The patient's neurological status has to be assessed hourly and Glasgow coma scale score should be calculated.
- Blood pressure and other vital parameters should be constantly monitored.
- Immediate non contrast CT Brain should be taken to find the cause of stroke. When ICH is the cause of stroke, the site and size of bleed is assessed to know the prognosis and plan further management.
- Laboratory investigations including the blood sugar, urea, creatinine, complete haemogram with coagulation studies and lipid profile have to be taken.

The prognosis and mortality of ICH patients can be assessed with ICH scoring system using age, haematoma volume, presence of intraventricular extension, infratentorial bleed and Glasgow coma scale score as variables. The minimal score is 0 and maximum score is 5. The 30 day mortality rate and the ability of patients to walk independently at 1 year are assessed by this scoring system.

TABLE. 2. ICH SCORING SYSTEM [2]

Clinical or Imaging Variable	Point
Age	
<80 years	0
>80 years	1
Haematoma Volume	
<30 cc	0
>30 cc	1
Intraventricular Haemorrhage	
No	0
Yes	1
Infratentorial Origin of Haemorrhage	
No	0
Yes	1
Glasgow Coma Scale Score	
13–15	0
5–12	1
3–4	2
Total Score	Sum of each category above

TOTAL ICH SCORE	DAY 30 MORTALITY (%)	Walk Independently at 1 YEAR (%)
0	0	70
1	13	60
2	26	33
3	72	3
4	97	8
5	100	None

MANAGEMENT OF INCREASED BLOOD PRESSURE[57]

The volume of haematoma generally increases with high blood pressure (BP). Most of the ICH patients have markedly increased BP during presentation. BP control in ICH should be done balancing for cerebral perfusion.

One important clinical trial INTERACT (INTENSIVE BLOOD PRESSURE REDUCTION IN ACUTE CEREBRAL HAEMORRHAGE TRIAL) assessed the goal of BP reduction in hypertensive ICH patients. They had two groups one with target level of Systolic BP (SBP) <180mmHg and another group with target of SBP < 140mmHg using

intravenous (IV) antihypertensives. They observed a statistical decrease in the haematoma growth and edema in those whose target SBP was <140mmHg. It is prudent to maintain Mean Arterial Pressure (MAP) <130mmHg. If facilities to monitor ICP are available then the target MAP reduction will be based on to maintain the Cerebral Perfusion Pressure (MAP-ICP) above 60mmHg.

Non vasodilating IV antihypertensive like nicardipine, esmolol or labetalol are preferred. The dose should be titrated periodically to maintain cerebral perfusion pressure.

MANAGEMENT OF INCREASED INTRACRANIAL PRESSURE (ICP) [58]

ICH most commonly causes raised Intra Cranial Pressure hence lowering it is important to prevent brainstem herniation. General measures to decrease ICP are control of hypertension and treatment of seizures.

Specific measures to decrease ICP are

- Hyperventilation following endotracheal intubation to achieve hypocapnea with pCO_2 in the range of 25 to 30 mm Hg.
- Use of intravenous mannitol (0.25-1 g/kg),
- Head end elevation
- Surgical decompression

SEIZURES[59]

Seizures are common with lobar ICH. Antiepileptic drugs are used for clinical seizures. It is necessary to control seizures in such patients in order to prevent further increase in ICP. But prophylactic anticonvulsants use is not justified.

ICH IN COAGULOPATHY

- When clotting factors deficiency is the cause of ICH patients should be treated with clotting factors replacement.
- When thrombocytopenia is the cause of ICH, patients should be treated with platelet transfusions.
- Protamine sulphate in doses of 1mg for 100 units of heparin is used in those who develop ICH as a complication of heparin treatment.
- For patients developing ICH as a complication of warfarin coagulopathy the following measures are done.
    - Warfarin should be stopped immediately
    - 5 to 25mg of Vitamin K is given IV and
    - Fresh frozen plasma (FFP) 10-20 ml/kg body weight or
    - Prothrombin complex concentrates are immediately transfused.
    - Recently recombinant factor VIIa injections have been used in warfarin coagulopathy related ICH.
- Cryoprecipitates, FFP and platelet transfusions are used in ICH related to thrombolytic therapy.

DEEP VEIN THROMBOSIS (DVT) PROPHYLAXIS:

Intermittent pneumatic compression along with elastic stockings is used in ICH patients to prevent DVT as a complication of prolonged immobilization.

MANAGEMENT OF GLUCOSE:

Blood glucose should be maintained in an optimal range.

TEMPERATURE MANAGEMENT

Hyperthermia is one of the important adverse prognostic factors in patients with ICH. Hence it is prudent to maintain the patient normothermic.

ROLE OF SURGERY [60,61]

SUPRATENTORIAL ICH

The International STICH (Surgical Trial of Intracerebral Haemorrhage) Trial was done to evaluate the outcome of 1033 cases of supratentorial ICH based on surgical and nonsurgical treatment.

The results of this trial showed that there was no superior benefit documented with either of the treatment modality but superficially located lobar haemorrhages were an exception. Lobar haemorrhages located superficially < 1 cm beneath the cortex and with haematoma volume around 20-40ml have a survival benefit from surgical evacuation of haematoma. STICH II trial is currently carried out to compare the outcome of surgical and nonsurgical treatments in superficial lobar ICH patients.

TREATMENT OF CEREBELLAR ICH[62]

In case of cerebellar ICH there is a clear cut benefit of outcome with those treated surgically compared to those treated conservatively.

- Cerebellar haematoma of size more than 3 cm in diameter definitely needs surgical evacuation.
- Those with haematoma size of less than 1 cm and preserved consciousness without brainstem compression, there is no need of surgical evacuation.
- For those with haematoma size between 1 to 3 cm, patients should be carefully monitored for signs of brainstem compression.

Surgical therapy is also done as an option to decrease intra cranial pressure in cases of cerebellar, caudate and thalamic ICH where there is massive hydrocephalus. Ventriculostomy provides drastic improvement by draining CSF and decreasing the intracranial tension.

SURGERY FOR VASCULAR MALFORMATIONS

Vascular malformations like Arterio Venous Malformations, cavernous angiomas and saccular aneurysms are important causes predisposing to ICH especially in young patients. So surgical treatment of these vascular malformations is important to prevent recurrent ICH in such patients.

RECURRENT ICH

Recurrence rate of ICH is around an average of 6%. The identification of cause of recurrent ICH is important. Among them the hypertensive bleeds are usually not associated with recurrent ICH, unless and otherwise there is poor control of blood pressure. AVM and cerebral amyloid angiopathy are associated with recurrent ICH. The site of recurrence of ICH also depends upon the cause of ICH. Hypertensive ICH presents with repeated basal ganglia bleeds. Non hypertensive causes like AVM and cerebral amyloid angiopathy present with repeated lobar bleeds.

PREVENTION OF RECURRENT ICH

Because of the high mortality of ICH it is always important to prevent another episode of ICH occurring among the survivors.

- First and foremost step is treating systemic hypertension.
- Avoidance of excessive use of alcohol.
- Prevention of use of sympathomimetic drugs.
- It is important to avoid the use of antithrombotic agents in those with amyloid angiopathy.
- Those with AVM or aneurysms should be treated surgically to prevent future recurrence.
- But data regarding restriction of use of statins or physical activity is insufficient.

FUTURE TRENDS IN ICH TREATMENT

Because of the limited treatment options available there is always a search for newer modalities of treatment for ICH. This leads to usage of procoagulants like the recombinant activated factor VIIa (rFVIIa).Use of recombinant factor VII a (rFVIIa)[63] in patients presenting with ICH within the first four hours slows the progression of bleeding and has been associated with smaller haematoma volumes but there was no clinical benefit. This was evaluated in FAST trial (Factor Seven for acute haemorrhagic Stroke Trial).

Recombinant factor VII a (rFVIIa) has been used in doses of 20 and 80 μg/kg in FAST trial. They found significant reduction in haematoma expansion in those treated with 80 μg/kg of recombinant factor VII a. But the risk of thrombo embolic complications was high. Moreover clinical benefits could not be documented well. So, few suggest the use of this agent in those showing signs of active bleed in CT Angiography like the dot sign. Further studies are needed regarding its use to document clear cut clinical benefit.

LIPIDS

The lipids are essential organic components of both the plant and animal kingdom. They provide fuel for multicellular organisms. They are stored in our body mainly in the adipose tissues and around the internal organs. From the biochemical point of view, lipids are complex group of substances like fats, steroids, oils etc. They are esters of various alcohols. Their most important property is that they are insoluble in water.

BIOLOGICAL SIGNIFICANCE OF LIPIDS[64,65]

- Lipids provide about 9.5 grams of calories for every gram on combustion, there by representing a concentrated source of fuel.
- They are important constituents of the cell membrane maintaining the integrity of the cells.
- They act as thermal insulators as they are present in subcutaneous adipose tissue.
- Lipids stored around the internal organs protect them from blunt injuries.
- With the help of lipids, the cytoplasm of cell in separated into various organelles.

- Lipids are the backbone for synthesis of steroidal hormones, bile acids and many cellular messengers like prostaglandins.
- Lipids provide essential fatty acids that are needed for normal growth.
- They form an integral part of human nervous system helping in its normal functioning.
- Vitamin A, D, E and K which are fat soluble are absorbed from the gut with the help of lipids.
- Lipids are conjugated with proteins to form lipoproteins which are transported in plasma.

A thorough knowledge of lipids is of prime importance as they are implicated in various diseases.

Bloor's criteria of lipids

Bloor established certain important characteristics of lipids

- Lipids are not soluble in water.
- They are soluble in certain solvents like ether which are called as fat solvents.
- Lipids combine with fatty acids to form esters.
- Lipids are used by living organisms.

LIPIDS CLASSIFICATION [66]

1. **Simple lipids** - These are esters of fatty acids combined with alcohols.

   i) **Fats:** Fats are triesters of fatty acid with alcohol. Fats occurring in liquid form are oils.

   ii) **Waxes:** These are fatty acid esters formed with high molecular weight alcohol which are aliphatic and monohydroxy.

2. **Complex lipids:**

   When esters of fatty acids have other substances along with alcohol and fatty acid they are called complex lipids.

   i) **Phospholipids:**

   Lipid substances possessing a phosphoric acid moiety along with fatty acid and alcohol are called phospholipids. These usually also contain nitrogen bases. E.g.) Lecithin- phosphatidyl choline, Cephalin, Sphingomyelin.

   ii) **Glycolipids (glycosphingolipids):**

   These lipids have a carbohydrate residue along with special alcohol known as sphingosine.

iii) **Other complex lipids:**

Sulfolipids and aminolipids have sulfate and aminoacid groups respectively. Lipoproteins have protein moieties in addition to lipids.

3. **Derived lipids**

These derived lipids are produced as a result of hydrolysis of simple or complex lipids. The substances in this category are

- Fatty acids-unsaturated or saturated fatty acids.
- Alcohol-straight chain alcohol, glycerol.
- Steroids-Cholesterol and other steroidal hormones.
- Vitamin A, D, E and K.

CHOLESTEROL[67,68]

The term cholesterol comes from a Greek word “chole steros” meaning “solid bile”. Cholesterol comes under the category of steroids. It is the most popular among steroids. Cholesterol occurs as white to yellow odorless granules. It is not soluble in water.

Many Nobel prizes have so far been awarded to cholesterol researchers. Michael Brown and Joseph Goldstein have quoted cholesterol in their literature as "the most highly decorated small molecule in biology."

DISCOVERY

- It was in 1769 cholesterol was first isolated.
- Francois Poulletier de la Salle was the first to discover cholesterol in bile and gallstones.
- Eugene Chevreul was the first person to understand the chemical components of cholesterol.
- In 1833 Boudet isolated cholesterol from blood.

STRUCTURE

The molecular formula of cholesterol is $C_{27}H_{45}OH$. Its structure has a cyclopentanoperhydrophenanthrene nucleus.

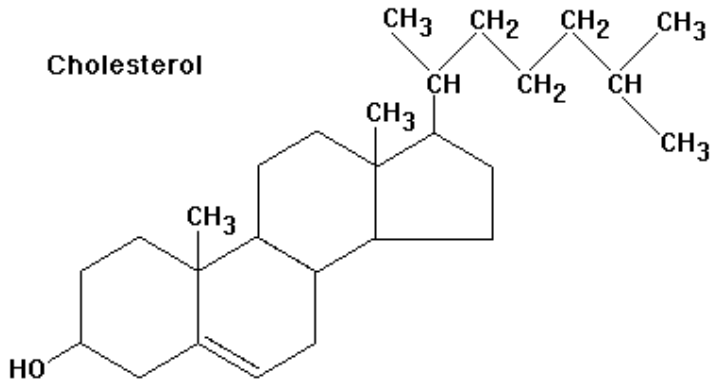


FIGURE.8.CHOLESTEROL STRUCTURE

The molecular structure of cholesterol was discovered by Heinrich Wieland and Adolf Windaus.

SOURCE OF CHOLESTEROL

EXOGENOUS SOURCE

Cholesterol is present in substances like milk, egg yolk, butter and meat i.e. mainly from animal sources. An average amount of cholesterol in our diet is around 0.3 gram per day. An average amount of cholesterol in a hen's egg is about 250mg.

ENDOGENOUS SOURCE

It is also synthesized from acetyl coA inside body approximately around 1gram per day.

OCCURRENCE IN BODY

Cholesterol is distributed in many tissues predominantly in the nervous system. It also occurs in liver, skin, gut mucosa and endocrine organs especially adrenal cortex. It is found in blood and also in bile.

CHOLESTEROL FORMS

There are two forms of cholesterol occurring in our body the free and the ester forms.

FREE FORM

Free cholesterol does not undergo esterification. It is the major form of cholesterol in human nervous system.

ESTER FORM

Adrenal cortex predominantly has the ester form of cholesterol. Here the cholesterol is esterified by combining with certain fatty acids at the C3 position of hydroxyl group. Linoleic acid, oleic acid, palmitic acid and arachidonic acids are the major fatty acids that esterify with cholesterol.

Majority of cholesterol esters are formed in plasma by the enzyme lecithin cholesterol acyl transferase (LCAT) that transfers acyl group from lecithin to cholesterol.

$$\text{LECITHIN+CHOLESTEROL} \xrightarrow{\text{LCAT}} \text{CHOLESTEROL ESTER+ LYSOLECITHIN}$$

Tissue acyl transferases form few cholesterol esters.

DIGESTION AND ABSORPTION

Cholesterol is absorbed predominantly as free form from the gut mucosa. Pancreatic enzyme cholesterol esterase helps in hydrolysis of cholesterol esters releasing the free form in the intestinal lumen. But later on the free forms are esterified within the intestinal cell to be transported as

cholesterol esters in the lymph. Unsaturated fatty acids and bile salts promote the absorption of cholesterol.

CHOLESTEROL METABOLISM [69,70,71,72]

SYNTHESIS[69]

Although all the human tissues are capable of synthesizing cholesterol, it is the liver that contributes as a major organ for synthesis. Skin, adrenals and intestine also form cholesterol. Some amount of synthesis also occurs in the muscle, adipose tissue and nervous system. Cytoplasm and endoplasmic reticulum are the major sites of cholesterol synthesis within the cell.

The carbon atoms of cholesterol are derived from Acetyl-CoA which is the starting molecule of cholesterol synthesis.

1) Acetyl Co-A with the help of two enzymes thiolase and HMG CoA synthase forms HMG CoA (3-hydroxy-3-methylglutaryl-CoA).

2) HMG CoA is converted to Mevalonate with the help of **HMG CoA reductase**. This step is the rate limiting step in the biosynthesis of cholesterol. Various factors influence the synthesis of cholesterol acting on this step. It is main target of therapeutic strategy to reduce cholesterol with statins.

Insulin and thyroxine increase the enzyme's action. While glucagon and glucocorticoids reduce its action. cAMP also reduces its action. This step requires NADPH as its cofactor.

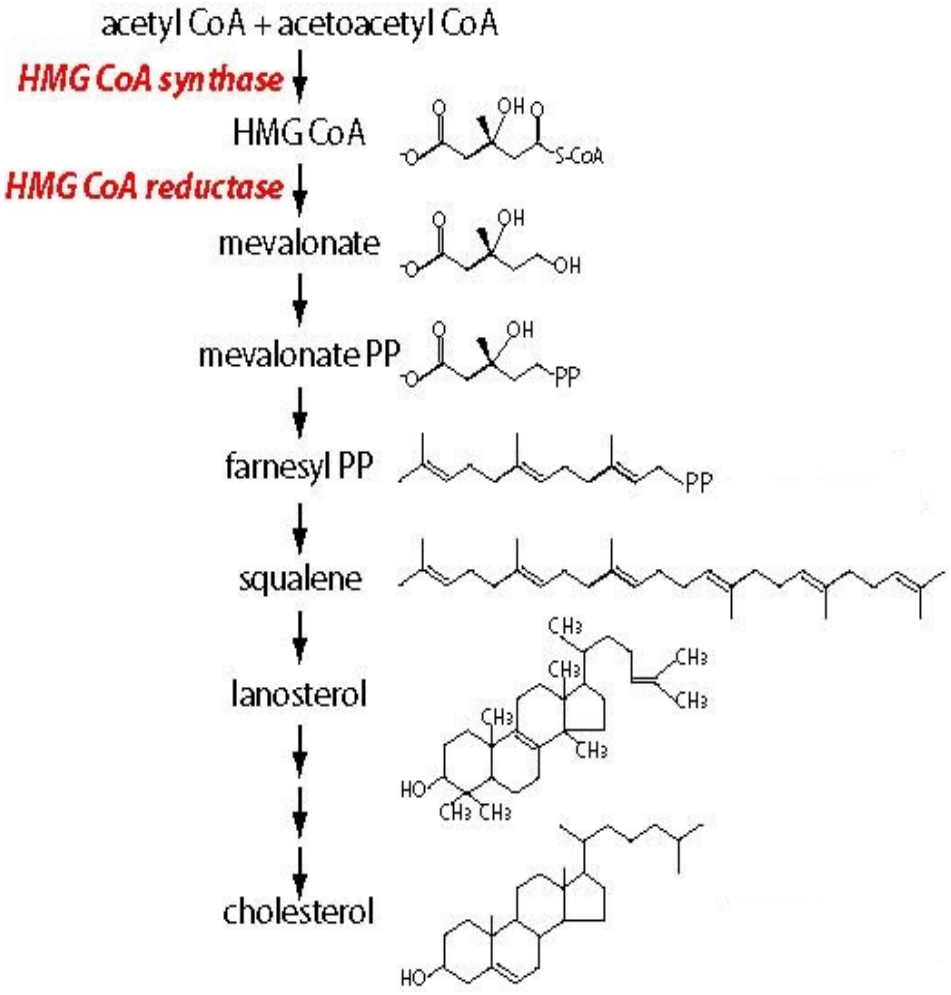


FIGURE.9.STEPS IN CHOLESTEROL SYNTHESIS

3) Phosphorylation of Mevalonate leads to formation of Mevalonate-5-Phosphate then Mevalonate-5-pyrophosphate and finally Mevalonate 3 phospho 5 pyrophosphate.

4) Mevalonate 3 phospho 5 pyrophosphate on decarboxylation forms Isopentenyl pyrophosphate.

5) Isopentenyl pyrophosphate on isomerization forms 3-3-dimethylallyl pyrophosphate.

6) By a series of reactions Geranyl diphosphate and Farnesyl diphosphate are formed.

7) Squalene is synthesized from two farnesyl diphosphate molecules by enzyme squalene synthase. Two molecules of farnesyl diphosphate condense at the diphosphate end to form squalene.

8) Lanosterol is derived from squalene by cyclization.

9) Cholesterol is formed from lanosterol by a series of steps forming 14-desmethyl lanosterol, zymosterol and desmosterol as intermediate molecules, by process of demethylation and reactions involving removal of $-CH_3$ group in the C_{14} position, shift of double bond between C_8 and C_9 to C_5 and C_6 and saturation of the double bond in the side chain.

CHOLESTEROL TRANSPORT

Dietary cholesterol is absorbed from the intestine along with other lipids and taken in chylomicrons and Very Low Density Lipoprotein (VLDL). 80-90% of absorbed cholesterol undergoes esterification in the lymph and transported predominantly as lipoproteins in plasma. Low Density lipoprotein (LDL) is the major lipoprotein carrying cholesterol to various tissues where it is taken up by them through the LDL receptor. Free cholesterol in plasma equilibrates with that in liver.

FACTORS INFLUENCING SERUM CHOLESTEROL LEVELS

Normal serum cholesterol varies from individual to individual [average of 200mg/dl is taken as cutoff value]. Numerous factors influence the serum cholesterol levels.

1. DIETARY LIPIDS[68]

Increased consumption of lipids especially saturated fatty acids increases the cholesterol synthesis. Poly unsaturated fatty acids in diet help to lower the serum cholesterol levels.

2. DIETARY CARBOHYDRATES

High intake of carbohydrates especially sucrose and fructose raise the serum cholesterol level.

3. HEREDITY

Genetic factors play a major role in serum cholesterol level variations.

4. BLOOD GROUPS

Blood group A individuals have higher serum cholesterol compared to those with group B or O.

5. DIETARY FIBRES

Increased intake of dietary fibers decreases the serum cholesterol by facilitating excretion of cholesterol and bile acids.

6. VITAMINS

Niacin in large amounts lowers serum cholesterol. Few animal studies have revealed that pyridoxine deficiency increases cholesterol level.

7. EXERCISE

Certain population studies have revealed that strenuous exercise decreases the cholesterol levels in serum.

FATE OF CHOLESTEROL

Most of the cholesterol in the body is eliminated in bile as free form or by conversion to bile acids. Cholic acid and chenodeoxy cholic acid are

the primary bile acids that are synthesized in the liver from cholesterol. They are then conjugated with glycine and taurine to be excreted in bile. These exist as salts in bile called bile salts. Some of the primary bile acids are converted to secondary bile acids deoxycholic acid and lithocholic acid by the gut bacteria. The bile acids undergo enterohepatic circulation and majority of them are reabsorbed in the terminal part of ileum. It is only a portion of the bile salts that is excreted in feces which is still the major route of cholesterol excretion.

OTHER FATES OF CHOLESTEROL

1. The adrenocortical hormones glucocorticoids and mineralocorticoids are derived from cholesterol.
2. 7-dehydrocholesterol in skin is converted to Vitamin D by ultraviolet rays which then by a series of reactions in liver and kidney is converted into active form of Vitamin D.
3. Sex hormones like androgens, estrogens and progesterones are formed from cholesterol.
4. Cholesterol in large intestine is converted to coprostanol and excreted in feces.
5. Cholesterol is important component of the cell membrane helping in cellular repair and proliferation.

LIPOPROTEINS[73,74,75]

The major vehicle of transportation of lipids in plasma is via lipoproteins. The main lipid groups found in lipoproteins are:

1. Cholesterol ester
2. Phospholipids
3. Triacylglycerol
4. Cholesterol esters
5. Unesterified fatty acids (free fatty acids)

Free fatty acids are the most active plasma lipids.

STRUCTURE[73]

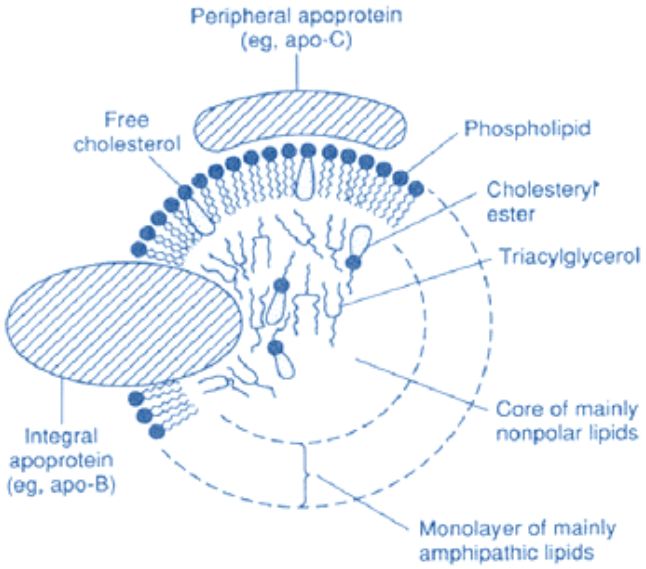


FIGURE 10.STRUCTURE OF LIPOPROTEIN

The structure of lipoprotein consists of hydrophobic core made up of nonpolar triacylglycerol and cholesterol esters. This is next enveloped by amphipathic phospholipids with their polar ends facing outside towards plasma. These are also complexed with apoproteins to form lipoprotein. As the content of lipid in the lipoprotein increases there is a decrease in the density of lipoprotein.

THE MAIN LIPOPROTEIN CLASSES ARE

1. Chylomicrons
2. Chylomicron Remnants
3. Very Low Density Lipoprotein(VLDL)
4. Intermediate Density Lipoprotein (IDL)
5. Low Density Lipoprotein(LDL)
6. High Density Lipoprotein(HDL)

The various classes of lipoproteins are arranged in decreasing order of size and in increasing order of their densities. Chylomicrons being the largest but least dense but HDL-C is the smallest in size with high density.

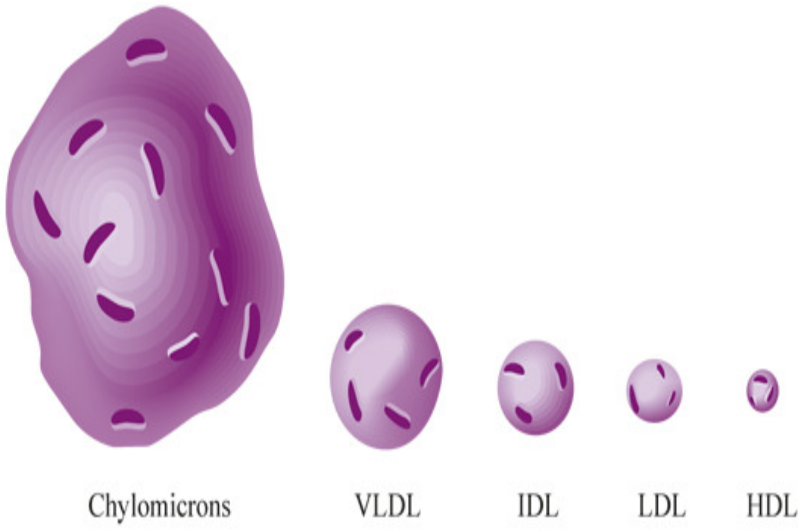


FIGURE.11.LIPOPROTEIN CLASSES

ELECTROPHORETIC CLASSIFICATION

Fredrickson classified lipoproteins based on their electrophoretic motility. Paper and agarose gel are most commonly used media.

The lipoproteins are classified as

- Origin- Chylomicrons
- Pre-β lipoprotein-VLDL
- β lipoprotein –LDL,IDL
- α lipoprotein –HDL

TABLE.3.LIPOPROPROTEIN CHARACTERISTICS

CLASS	DENSITY (g/ml)	ELECTRO-PHORESIS	SOURCE	CHIEF LIPID	APOPROTEIN
Chylomicron	< 0.95	Origin	Intestine	85% Triglyceride (TGL)	B48, AI, AIV (E, CI, CII, CIII—by transfer from HDL)
Chylomicron remnants	<1.006	Origin	Intestine	60% TGL, 20% CHOL	B48, E
VLDL	<1.006	Pre-β	Liver	55% TGL, 20% CHOL	B100, E, CI, CII, CIII
IDL	1.006-1.019	β	Derived from VLDL	35% CHOL, 25% TGL	B100, E
LDL	1.019-1.063	β	Derived from IDL	60% CHOL, 5% TGL	B100
HDL	1.063-1.21	α	Liver, intestine, plasma	25% PL 20% CHOL, 5% TGL 50%-protein	AI, AII, CI, CII, CIII, E
HDL_2	1.063-1.125	α			
HDL_3	1.125-1.21	α			
Lp(a)	1.05-1.09	α	Liver	60% CHOL 5% TGL	B100, apo(a)

Very Low Density Lipoprotein (VLDL);

Intermediate Density Lipoprotein (IDL);

Low Density Lipoprotein (LDL);

High Density Lipoprotein (HDL)

CHOL-Cholesterol;

TGL-Triglyceride

PL-Phospholipids

METABOLISM OF LIPOPROTEINS [75]

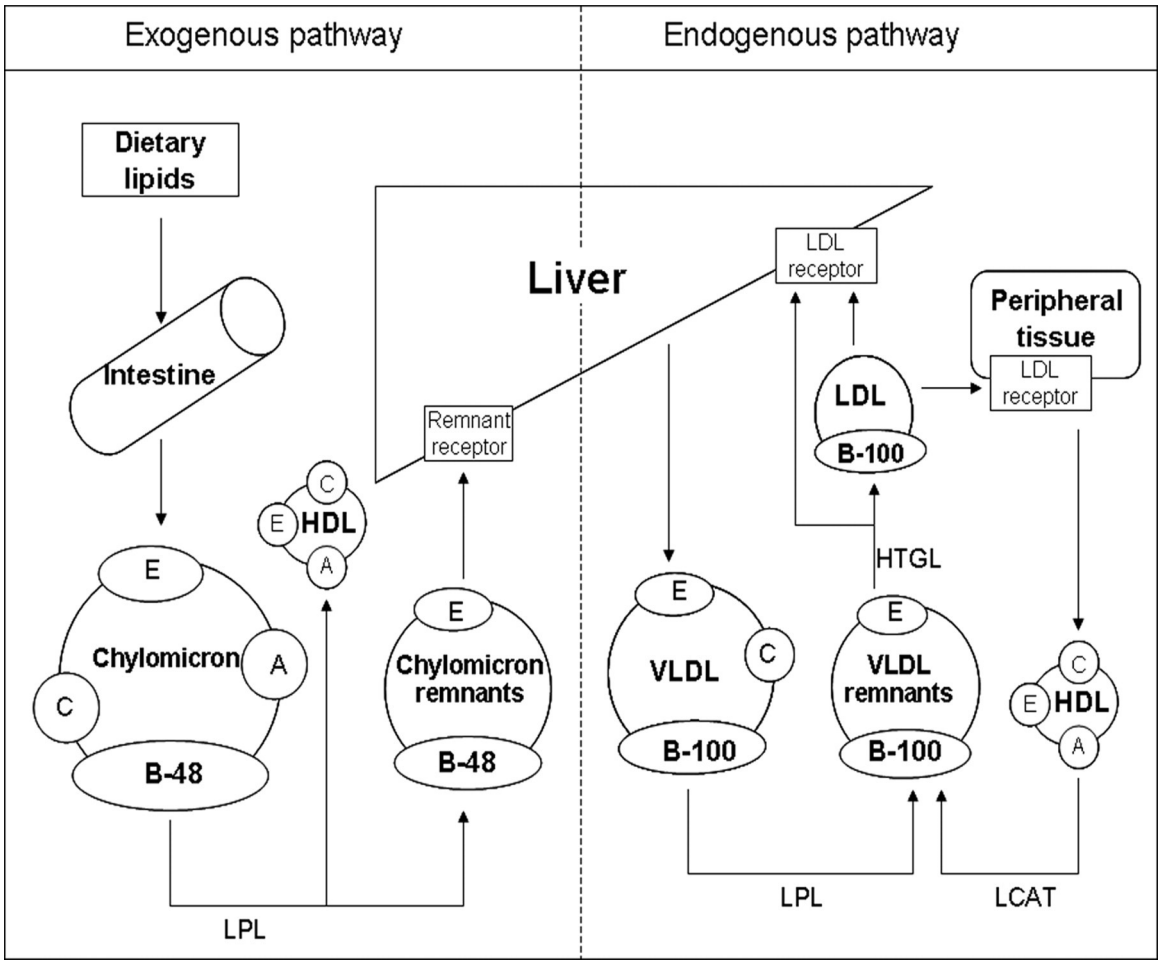


FIGURE.12.METABOLISM OF LIPOPROTEINS

SOURCES OF LIPOPROTEINS

1. Chylomicrons are obtained as a result of absorption of the triacylglycerol from intestine (i.e. exogenous).

2. VLDL is obtained by endogenous synthesis in liver.

3. LDL is obtained as a result of degradation of VLDL.

4. HDL is obtained from synthesis in liver and intestinal cells.

TRANSPORT OF TRIACYLGLYCEROL

Chylomicrons are the major vehicle of transportation of exogenous triacylglycerol that is absorbed from intestine as a result of fat digestion. They are seen in the chyle of the intestinal lymphatics transporting lipids of dietary origin to the circulation. VLDL is the major carrier of endogenous triacylglycerol from liver to other tissues.

The chylomicrons initially have apo B48, apo AI and apo AIV. They later on get the apo E and apo C components from HDL in plasma. VLDL initially has apo B100, apo E and some apo C. They later on get apo E and apo C components from HDL in plasma.

CATABOLISM

Shortly after their formation the chylomicrons and VLDL undergo rapid catabolism and form chylomicron remnants and IDL respectively. Most of the fatty acids that are brought by catabolism of the triacylglycerol are taken to the adipose tissue, skeletal and cardiac muscles while some go to liver.

THE ACTION OF LIPOPROTEIN LIPASE

Lipoprotein lipase situated in the capillary wall is attached to the endothelium with the help of heparan sulphate. Hepatic lipase is situated in the liver cells at the surface of sinusoids. The important cofactors needed for the action of these enzymes are phospholipid and apo CII but apo A II and apo CIII are the inhibitors of this enzyme. Lipoprotein lipase hydrolyses the lipoproteins especially the triacylglycerol into diacylglycerol then to monoacylglycerol and ultimately form free fatty acids and glycerol. Among the free fatty acids, few enter the circulation while a great amount of fatty acids are taken to other tissues.

The fatty acids from VLDL are taken to fat cells by binding to the VLDL receptor. The synthesis of lipoprotein lipase in adipose tissue is increased by insulin.

The lipoprotein lipase acting on chylomicrons removes most of triacylglycerol and apo C retaining apo E resulting in formation of chylomicron remnants which have higher content of cholesterol and their esters. In the same manner, VLDL is metabolised to form VLDL remnant i.e. IDL (INTERMEDIATE DENSITY LIPOPROTEIN).

THE REMNANT LIPOPROTEINS UPTAKE

The major organ that plays role in the remnant lipoprotein uptake is liver. This is by receptor mediated endocytosis. After that the cholesterol esters and remaining triacylglycerol are catabolised. Hepatic lipase plays a role in this step. Receptor mediated endocytosis of IDL occurs in liver and leads to formation of LDL.

CATABOLISM OF LDL

The most important step in metabolism of LDL is its uptake by liver (70%) and extrahepatic tissues (30%) by LDL receptor (apo B100, apo E) . LDL is the major carrier of cholesterol from liver to extrahepatic cells. Because of this LDL is considered as bad cholesterol promoting atherogenesis . Based on the hepatic influx of free fatty acids the synthesis of LDL is increased. Any defect in the LDL receptor that reduces its action causes decreased catabolism of LDL increasing its plasma levels.

HDL METABOLISM[76]

HDL is mainly synthesized by liver. It has apo C and apo E which are important in the catabolism of both chylomicrons and VLDL. Initially formed HDL is discoidal with phospholipids, apo A and cholesterol. The binding of lecithin cholesterol acyltransferase (LCAT) and apo AI, the activator of LCAT to the discoidal HDL helps in conversion of free cholesterol to cholesterol esters and lysolecithin. This leads to formation of nonpolar lipid core and polar groups outside there by changing the HDL form to spherical and pseudo micelle type.

Scavenger receptor B 1(SRB1) is the HDL receptor[77, 78]. SRB1 receptor in liver binds to HDL and causes transfer of cholesterol esters to the hepatocytes. In extrahepatic tissues it modifies HDL making it a major acceptor of cholesterol thereby transporting cholesterol from other tissues to liver. This cholesterol is later on excreted into bile. Hence HDL is called good cholesterol. This process is known as reverse cholesterol transport. HDL-C is hence anti atherogenic.

It is HDL3 that is initially formed; this is converted to less dense HDL2 after it accepts the extrahepatic cholesterol through SRB1 receptor. Later on HDL3 is formed again by HDL2 hydrolysis.The transformation between HDL 3 and HDL2 is known as HDL cycle. Pre β HDL is formed

after apo AI is released and some amount of phospholipids and cholesterol are added.

- ATP binding cassette transporters A1 [ABCA1] & G1 [ABCG1] mediate another important mechanism in the process of reverse cholesterol transport.
- Cholesterol Ester Transfer Protein (CETP) transfers cholesteryl esters from HDL to the lower density lipoproteins.CETP has a major role in lipid metabolism and can influence the process of atherogenesis.

Because of the reverse cholesterol transport HDL when present in higher concentrations exert anti atherogenic effect decreasing the incidence of coronary artery heart disease. HDL also has antioxidant property.

ROLE OF LIPIDS IN DISEASES[79]

- Elevated serum cholesterol had been established as a major risk factor in the pathogenesis of atherosclerosis and hence associated with increased incidence of ischemic heart disease and cerebral infarction.
- Diseases like diabetes, hypothyroidism and renal diseases which are characterized by secondary hyperlipidemia also accelerate atherosclerosis.
- HDL-Cholesterol is known for its negative correlation[76] with atherosclerosis because of its reverse cholesterol transport.

- Fredrickson classified the primary hyperlipoproteinemias into five different classes based on the major classes of lipoproteins elevated and different genetic mutations.

Fredrickson Classification of Hyperlipoproteinemias

Phenotype	I	IIa	IIb	III	IV	V
Lipoprotein, elevated	Chylomicrons	LDL	LDL and VLDL	Chylomicron and VLDL remnants	VLDL	Chylomicrons and VLDL
Triglycerides	↑↑↑	N	↑	↑↑	↑↑	↑↑↑
Cholesterol (total)	↑	↑↑↑	↑↑	↑↑	N/↑	↑↑
LDL-cholesterol	↓	↑↑↑	↑↑	↓	↓	↓
HDL-cholesterol	↓↓↓	N/↓	↓	N	↓↓	↓↓↓
Plasma appearance	Lactescent	Clear	Clear	Turbid	Turbid	Lactescent
Xanthomas	Eruptive	Tendon, tuberous	None	Palmar, tuberoeruptive	None	Eruptive
Pancreatitis	+++	0	0	0	0	+++
Coronary atherosclerosis	0	+++	+++	+++	+/–	+/–
Peripheral atherosclerosis	0	+	+	++	+/–	+/–
Molecular defects	LPL and ApoC-II	LDL receptor, ApoB-100, PCSK9, LDLRAP, ABCG5 and ABCG8		ApoE	ApoA-V	ApoA-V and GPIHBP1
Genetic nomenclature	FCS	FH, FDB, ADH, ARH, sitosterolemia	FCHL	FDBL	FHTG	FHTG

Abbreviations: ADH, autosomal dominant hypercholesterolemia; Apo, apolipoprotein; ARH, autosomal recessive hypercholesterolemia; FCHL, familial combined hyperlipidemia; FCS, familial chylomicronemia syndrome; FDB, familial defective ApoB; FDBL, familial dysbetalipoproteinemia; FH, familial hypercholesterolemia; FHTG, familial hypertriglyceridemia; LPL, lipoprotein lipase; LDLRAP, LDL receptor associated protein; GPIHBP1, glycosylphosphatidylinositol-anchored high density lipoprotein binding protein1; N, normal

FIGURE.13. HYPERLIPOPROTEINEMIAS FREDRICKSON CLASSIFICATION

SECONDARY HYPERLIPIDEMIAS

- Diabetes mellitus
- Hypothyroidism
- Renal diseases like nephrotic syndrome and end stage renal disease
- Hepatitis and cholestasis
- Cushing's syndrome
- Lysosomal storage disorders
- Estrogen and certain drugs like steroids and thiazides.

The above mentioned conditions are associated with elevation of various lipid levels promoting atherogenesis. There are many classes of lipid lowering agents used in clinical practice to control hyperlipidemias.

LIPID LOWERING DRUGS	INDICATIONS
HMG-CoA Reductase Inhibitors (Statins): Atorvastatin, Lovastatin, Simvastatin, Pravastatin.	Elevated LDL-C
Bile acid sequestrants: Cholestyramine, Colestipol	Elevated LDL-C
Fibric acid derivatives Gemfibrozil,Fenofibrate	Elevated TGL

LIPID LOWERING DRUGS	INDICATIONS
➢ Nicotinic acid	Low HDL-C; Elevated TGL; LDL-C
➢ Omega 3 fatty acids	Elevated TGL
➢ **Cholesterol absorption inhibitors** Ezetimibe	Elevated LDL-C

DISORDERS ASSOCIATED WITH HYPOLIPIDEMIAS

Few conditions are associated with low levels of certain lipid fractions. They are frequently inherited causes. Few are mentioned below.

I) CONDITIONS WITH LOW LEVELS OF APOB LIPOPROTEINS

Familial Hypobetalipoproteinemia

Low plasma levels of LDL-C due to mutations in apoB.

PCSK9 [proprotein convertase subtilisin/kexin type 9] Deficiency

Loss of function mutation of PCSK9 with low levels of LDL-C.

Abetalipoproteinemia

Abetalipoproteinemia is due to mutation in microsomal triglyceride transfer protein gene resulting in low cholesterol, triglycerides and β lipoproteins.

II) INHERITED CAUSES OF LOW LEVELS OF HDL-C

Gene Deletions and Mutations in Apo A-I

Tangier's Disease

Mutations in the gene encoding ABCA1

LCAT Deficiency

Due to deficiency of lecithin cholesterol acyl transferase there is impaired maturation of HDL.

Primary Hypoalphalipoproteinemia

It is characterized by low HDL-C.

NATIONAL CHOLESTEROL EDUCATION PROGRAM ATP III GUIDELINES FOR MANAGEMENT OF LIPID DISORDERS[80,81,82]

- **TOTAL CHOLESTEROL**
  - <200 mg/dl - Desirable
  - 200-239 mg/dl - Borderline high
  - ≥240 mg/dl - High

- **LDL CHOLESTEROL**
  - <100 mg/dl - Optimal
  - 100-129 mg/dl - Near optimal
  - 130-159 mg/dl - Borderline high
  - 160-189 mg/dl - High
  - ≥190 mg/dl - Very high

- **TRIGLYCERIDES**
  - <150 mg/dl - Normal
  - 150-199 mg/dl - Borderline high
  - 200-499 mg/dl - High
  - ≥500 mg/dl - Very high

- **HDL CHOLESTEROL**
  - <40 mg/dl - Low
  - ≥60 mg/dl - High

LOW CHOLESTEROL AND INTRACEREBRAL HAEMORRHAGE

Many population based studies like the MRFIT study and HONOLULU HEART PROGRAM have shown that low serum cholesterol is associated with intracerebral haemorrhage. This paradox of inverse association of serum cholesterol and ICH is more pronounced with cholesterol levels especially when less than 160mg% according to the MRFIT study.

The proposed theory for this inverse association is as follows. Cholesterol and triglycerides are needed for normal cell membrane integrity especially the vascular endothelial cells. Low levels of these lipids may cause increased erythrocyte fragility and weakening of the capillary endothelium leading to micro aneurysms and promote intracerebral haemorrhage especially in those with systemic hypertension. This inverse association of serum lipids with ICH forms the background of our study.

MATERIALS AND METHODS

SOURCE OF DATA

A total number of 50 patients who presented with Intracerebral Haemorrhage during the study period from December 2013 to August 2014 in Thanjavur Medical College Hospital and who fulfilled the inclusion criteria were taken for the study.

PLACE OF STUDY:

Thanjavur Medical College Hospital, Thanjavur.

STUDY DESIGN:

Single centre hospital based prospective observational study.

INCLUSION CRITERIA:

Patients admitted in Thanjavur Medical College Hospital with Intracerebral Haemorrhage (ICH).

EXCLUSION CRITERIA:

1. Traumatic Intracerebral Haemorrhage.(ICH)
2. Subarachnoid haemorrhage
3. Tumour Bleed
4. Use of Anticoagulants, Use of Antiplatelets, Use of Statins.

5. Intracranial Aneurysm, AV Malformations

6. Sympathomimetics abuse

7. History of bleeding diathesis

8. Patients with thrombocytopenia

METHODS OF COLLECTION OF DATA:

50 patients with Intracerebral Haemorrhage satisfying inclusion criteria admitted in Thanjavur Medical College Hospital from December 2013 to August 2014 were taken for the study after excluding those who had features given in exclusion criteria. After obtaining consent, history, clinical examination and investigations were done.

Diagnosis of Intracerebral haemorrhage was made in patients based on history, clinical features and plain non contrast CT scan of Brain.

INVESTIGATIONS DONE

1) Blood sugar

2) Blood urea

3) Serum creatinine

4) Serum electrolytes- Sodium and potassium

5) Urine albumin, sugar and deposits

6) Complete haemogram including

- Haemoglobin,
- Total WBC count, differential counts,
- Red cell count,
- Platelet count,
- Peripheral smear
- Erythrocyte Sedimentation Rate (ESR)
- Bleeding time, Clotting time,
- Prothrombin Time and Activated Partial Thromboplastin Time (PT, aPTT)

7) Fasting Lipid Profile-

Total Cholesterol (TC),

Low density cholesterol (LDLc),

High density cholesterol (HDLc) ,

Very Low density cholesterol (VLDLc) and

Triglycerides (TG)

8) ECG

9) CT Brain

10) Other investigations like MRI brain with MR angiography, Ultrasound abdomen, Chest X ray, Echocardiography and Liver Function Tests were taken .

LIPID PROFILE ESTIMATION

Blood was collected for lipid profile estimation from the ICH patients within 24 to 48 hours of onset of disease. The sample was collected after 9 to 12 hours of fasting.

The serum was separated and was subjected to centrifugation .The supernatant was taken out and subjected for analysis.

ESTIMATION OF CHOLESTEROL

Serum cholesterol was estimated by the **calorimetric method CHOD-POD**. It is based on the principle that cholesterol produces a coloured complex during the CHOD-POD reaction and the absorbance of the coloured complex assessed by calorimeter is directly proportional to the concentration of cholesterol in that sample.

$$\text{Cholesterol Ester} + \text{Water} \xrightarrow{\text{CHE}} \text{Cholesterol} + \text{Fatty Acid}$$

$$\text{Cholesterol} + \text{Oxygen} \xrightarrow{\text{CHO}} \text{4-Cholestenone} + H_2O_2$$

$$2H_2O_2 + \text{4-Aminoantipyrine} + \text{Phenol} \xrightarrow{\text{POD}} \text{Quinoneimine dye} + 4H_2O$$

CHE-Cholesterol Esterase

CHOD-Cholesterol Oxidase

POD-Peroxidase

$$\frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} \times \text{Standard concentration} = \text{mg/dL cholesterol}$$

ESTIMATION OF HIGH DENSITY CHOLESTEROL (HDL-C)

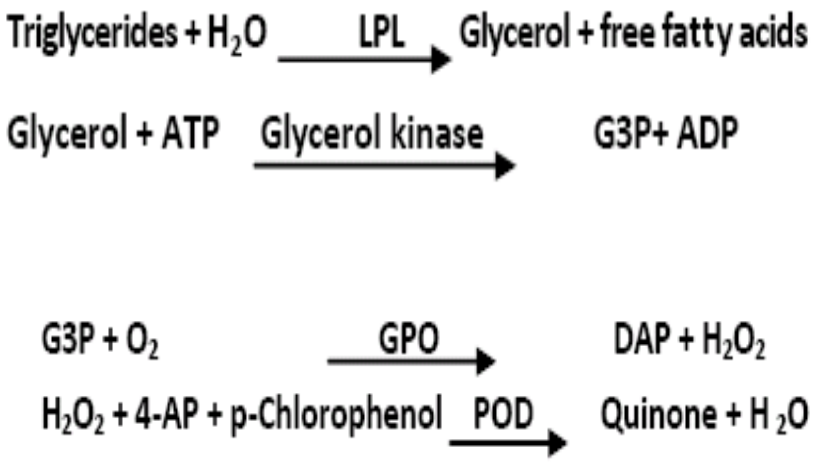
It is based on the principle that very low density (VLDL) and low density (LDL) cholesterol in the sample are precipitated when mixed with phosphotungstic acid along with magnesium ions and on subjecting to centrifugation the concentration of HDL cholesterol can be determined in the sample by calorimetric method.

$$\frac{\text{Abs of Sample} \times \text{Standard concentration} \times \text{dilutional factor}}{\text{Abs of Standard}} = \text{HDL–C in mg/dl}$$

ESTIMATION OF TRIGLYCERIDES (TGL)

The sample to be tested for triglycerides is treated with lipoproteinlipase (LPL) where it gives glycerol and free fatty acids. By the action of glycerol kinase and ATP glycerol is converted to glycerol-3-phosphate (G3P) and adenosine-5-diphosphate (ADP).

Glycerol phosphate dehydrogenase [GPO] converts Glycerol-3-phosphate [G3P] to dihydroxyacetone phosphate [DAP] and hydrogen peroxide [H2O2]. Peroxidase [POD] catalyses the reaction of hydrogen peroxide [H2O2] with 4-aminophenazone and p-chlorophenol to form coloured compound.



The absorbance of the coloured complex assessed by calorimeter is directly proportional to the concentration of triglycerides in that sample.

$$\frac{\text{Absorbance of Sample X Standard concentration}}{\text{Absorbance of Standard}} = \text{mg/dL TGL in sample}$$

ESTIMATION OF LDL-CHOLESTEROL

The Friedewald Formula is used for indirect estimation of serum LDL.

$$\text{LDL cholesterol} = \text{Total cholesterol} - \frac{[\text{HDL} + \text{TGL}]}{5}$$

ESTIMATION OF VLDL-C

$$\text{VLDL-C} = \frac{\text{TRIGLYCERIDE}}{5}$$

The details of the patient like history, clinical examination and investigations were collected and entered in a proforma sheet. The model of the proforma used has been enclosed as an annexure.

ANALYSIS:

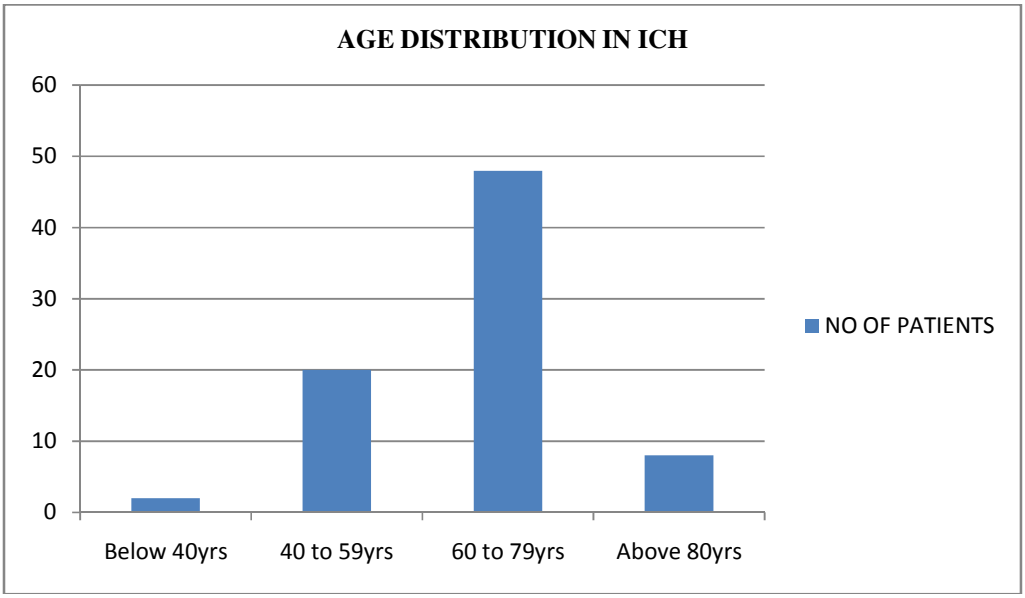
The statistical analysis of the data collected from the patient was done using SPSS (Statistical Package for Social Sciences) software.

OBSERVATION AND RESULTS

TABLE.4. AGE DISTRIBUTION IN PATIENTS

AGE	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
Below 40 yrs	2	4.0
40 to 59 yrs	20	40.0
60 to 79 yrs	24	48.0
Above 80 yrs	4	8.0

FIGURE.14.AGE DISTRIBUTION IN PATIENTS



The mean age group of this study is 59.1 (± 12.61) years.

In this study among the 50 patients of Intracerebral Haemorrhage ,

48% belong to age group of 60-79years

40% belong to age group of 40-59years.

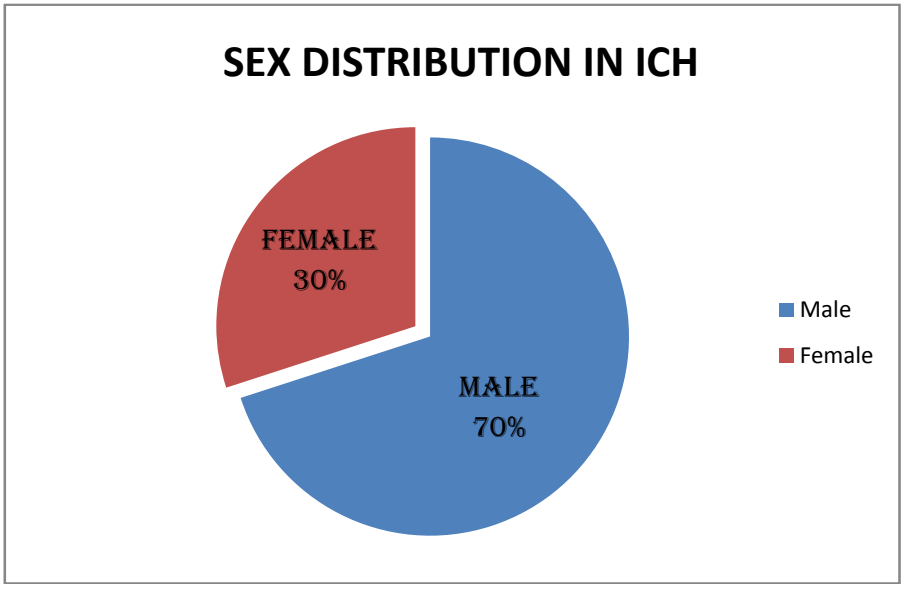
8% belong to above 80 years.

4% belong to below 40 years.

TABLE.5.SEX DISTRIBUTION IN PATIENTS

SEX	NO.OF PATIENTS (n=50)	PERCENTAGE (100%)
Male	35	70.0
Female	15	30.0

FIGURE.15.SEX DISTRIBUTION IN PATIENTS



70% of ICH patients in our study are males;

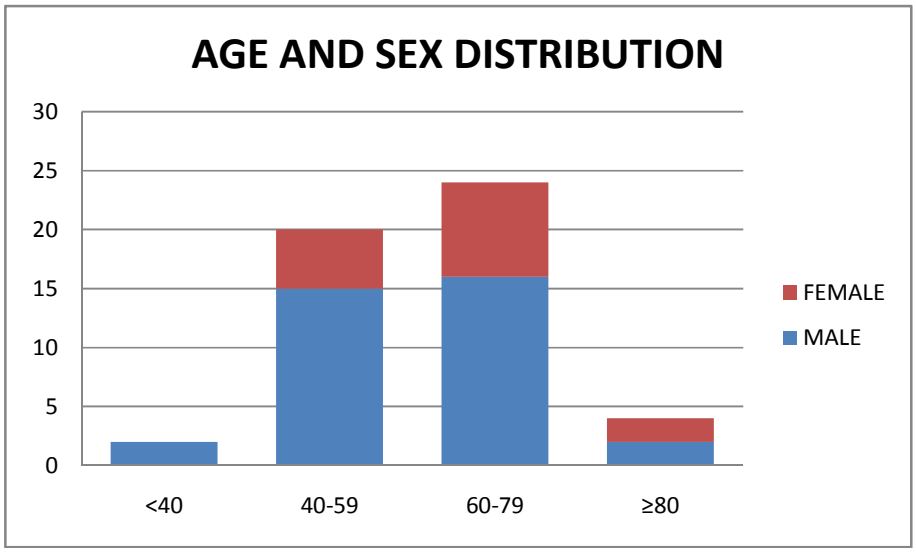
30 % of ICH patients are females in our study.

The male: female ratio is 2.3: 1.

TABLE.6.AGE AND SEX DISTRIBUTION OF ICH

AGE	MALES	FEMALES
Below 40 yrs	2	0
40 to 59 yrs	15	5
60 to 79 yrs	16	8
Above 80 yrs	2	2

FIGURE.16.AGE AND SEX DISTRIBUTION IN PATIENTS



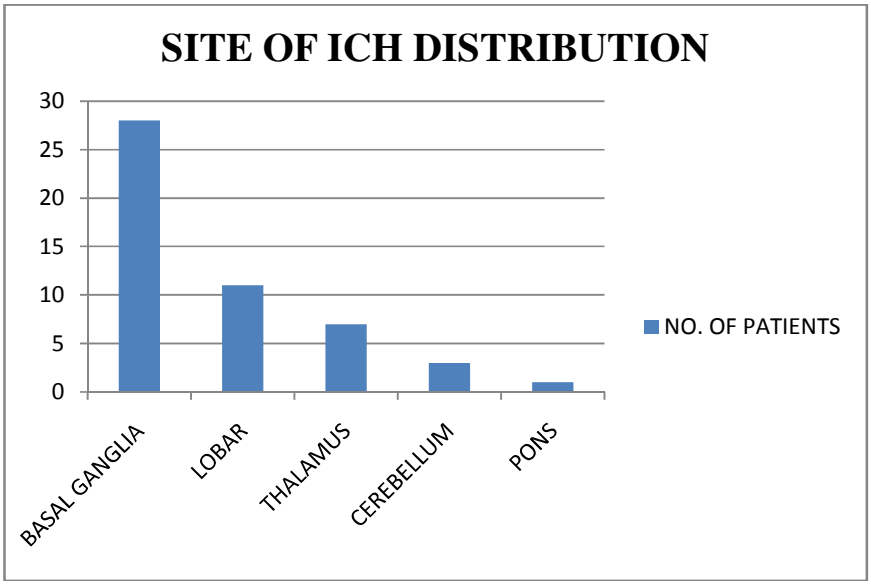
The mean age group among the male patients with ICH was 58 years.

The mean age group among the female patients with ICH was 62 years.

TABLE.7.SITE OF ICH DISTRIBUTION

SITE OF ICH	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
BASAL GANGLIA	28	56.0
LOBAR	11	22.0
THALAMUS	7	14.0
CEREBELLUM	3	6.0
PONS	1	2.0

FIGURE.17.SITE OF ICH DISTRIBUTION



Basal ganglia constitutes the most common site of ICH in our study, contributing to 56% of cases.

Lobar ICH is the second most common site accounting for 22% of patients.

Thalamic haemorrhage contributes to about 14% of patients.

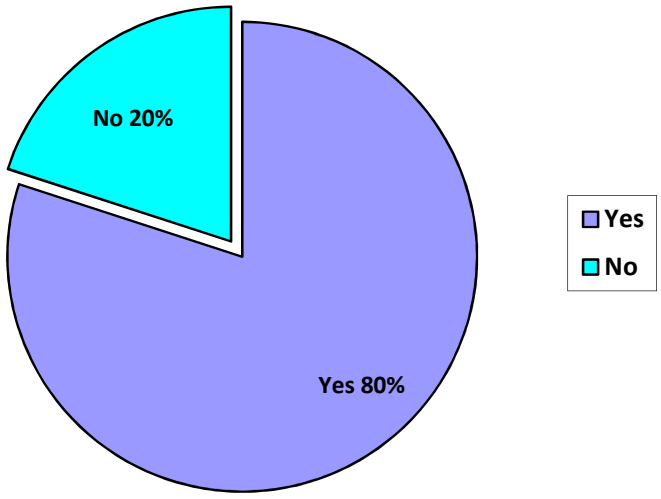
Cerebellar bleeds were 6 % of the total cases.

Pons was the site of ICH only in 2 % of study group.

TABLE.8. SHT IN PATIENTS

SHT	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
Yes	40	80.0
No	10	20.0

FIGURE.18.SHT IN PATIENTS



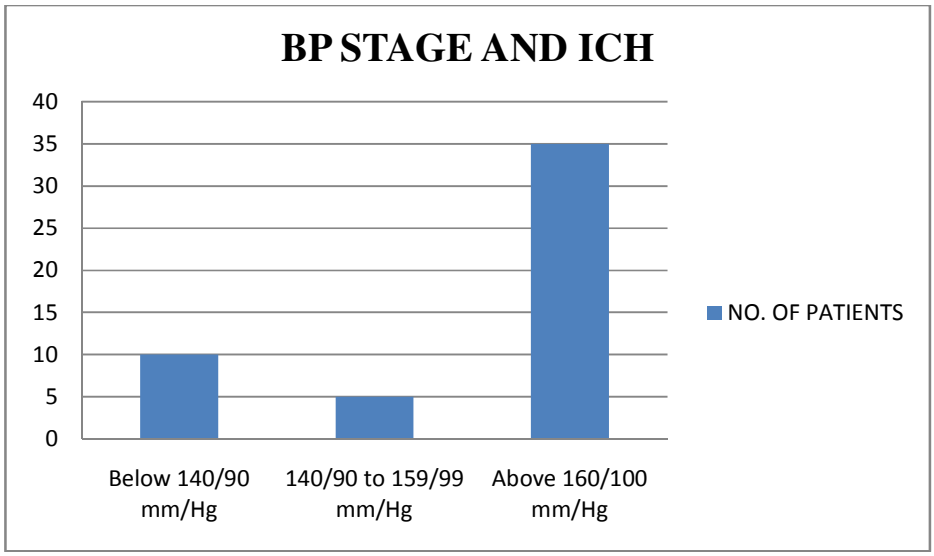
A clear majority of ICH patients around 80% are hypertensives in our study.

Only 20% of the patients are non hypertensives.

TABLE.9.BP STAGE IN PATIENTS

BP STAGE (mmHg)	NO.OF RESPONDENTS (N=50)	PERCENTAGE (100%)
Below 140/90	10	20.0
140/90 to 159/99	5	10.0
Above 160/100	35	70.0

FIGURE.19.BP STAGE IN PATIENTS



Around 70% of the total ICH patients in our study had Stage II hypertension (BP ≥ 160/100 mmHg).

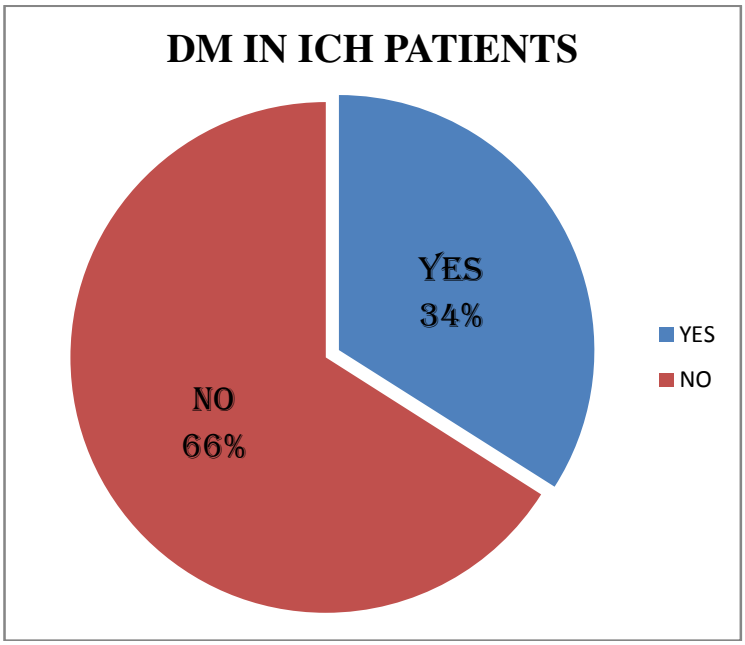
10% of patients had Stage I hypertension (BP 140/90 -159/99 mm Hg).

As mentioned earlier 20% had BP <140/90 mmHg.

TABLE.10.DM IN ICH PATIENTS

DM	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
Yes	17	34.0
No	33	66.0

FIGURE.20.DM IN ICH PATIENTS



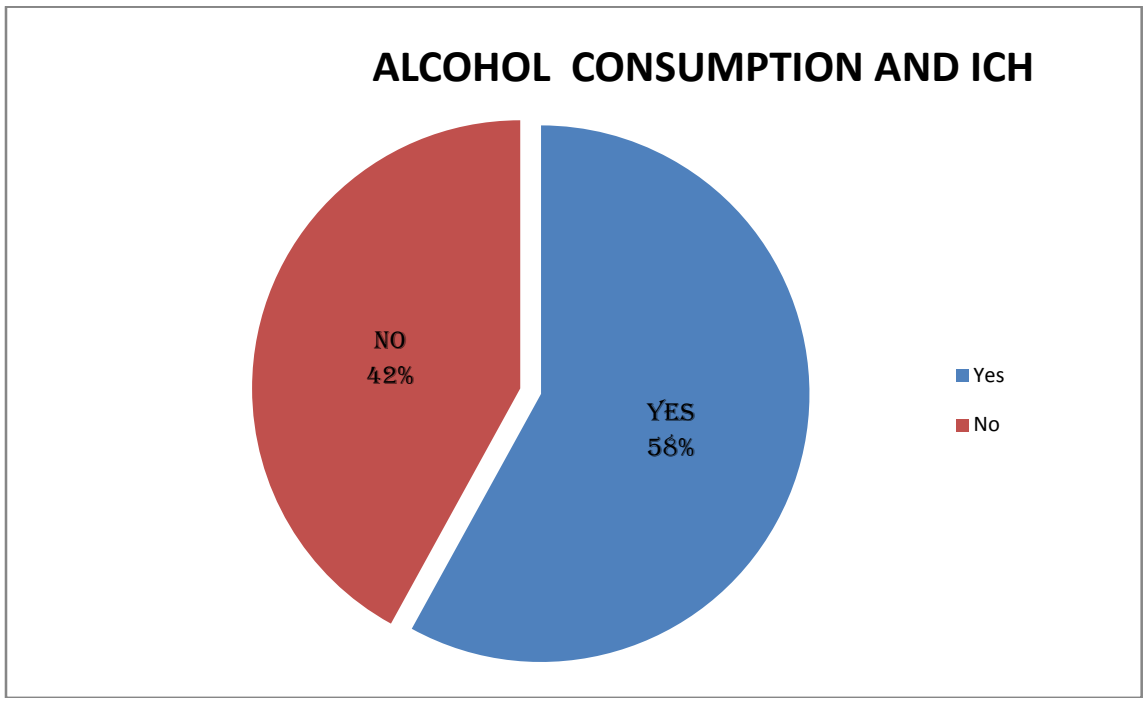
Only 34 % of patients in our study had diabetes mellitus.

66% did not have diabetes mellitus.

TABLE.11.ALCOHOL CONSUMPTION IN PATIENTS

ALCOHOL	NO. OF PATIENTS (n=50)	Percentage (100%)
Yes	29	58.0
No	21	42.0

FIGURE.21.ALCOHOL CONSUMPTION IN PATIENTS



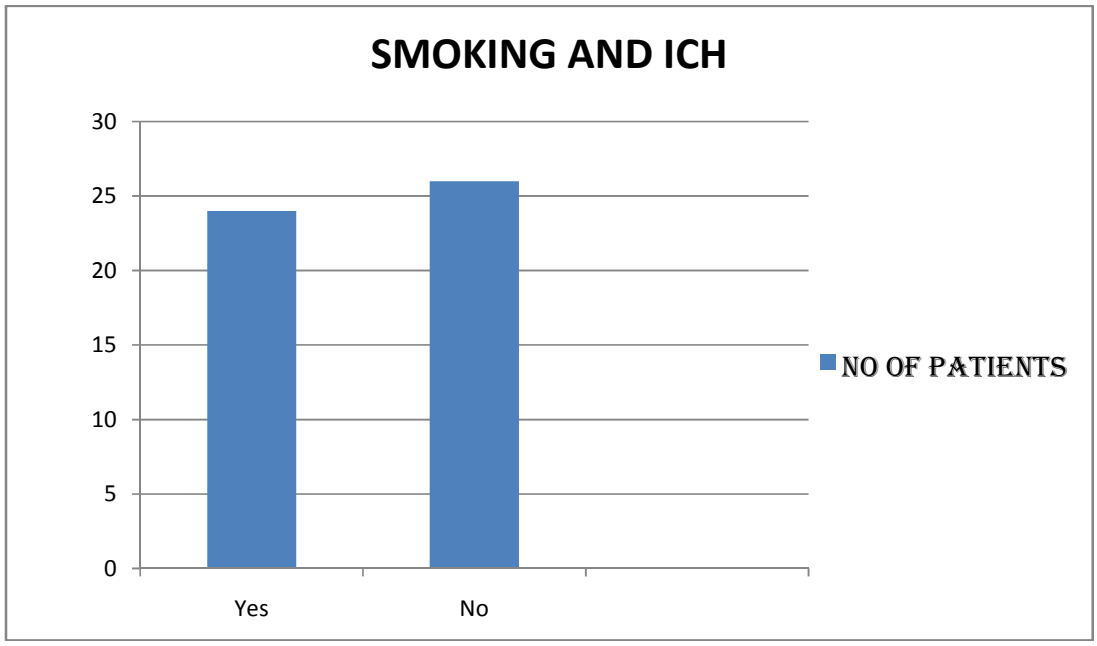
58% of patients in our study had history of alcohol consumption.

42% of the patients were non alcoholics.

TABLE.12.SMOKING IN PATIENTS

SMOKING	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
Yes	24	48.0
No	26	52.0

FIGURE.22.SMOKING IN PATIENTS



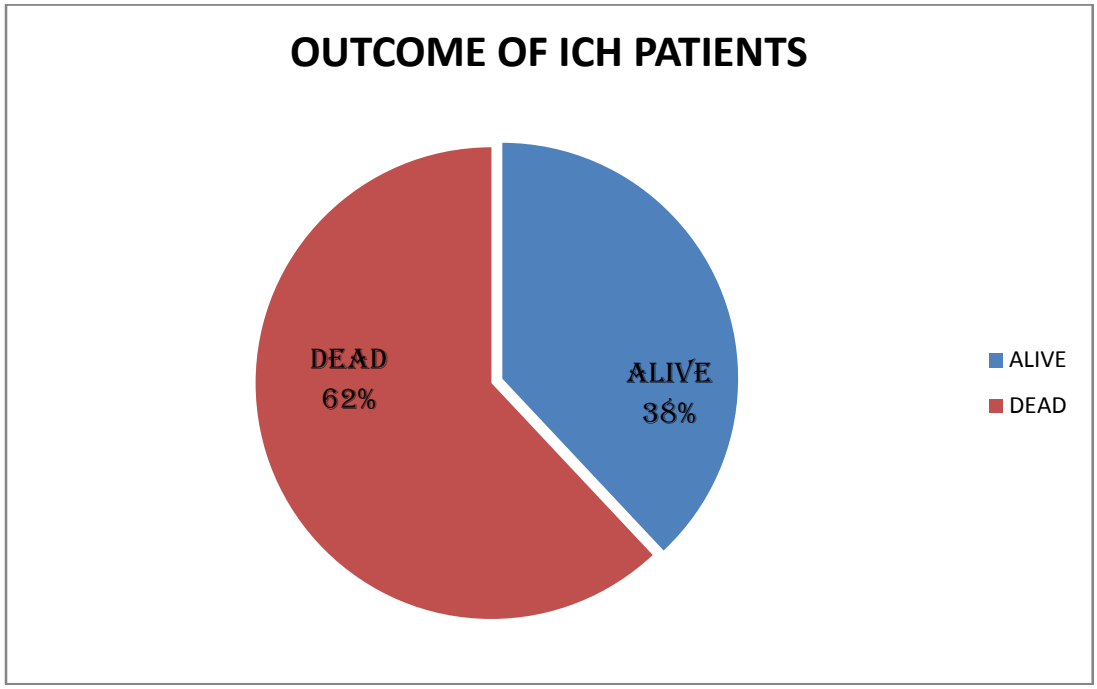
About 52% of patients in our study group are nonsmokers.

Only 48% of patients in our study are smokers.

TABLE.13.OUTCOME OF ICH PATIENTS

OUTCOME	NO.OF PATIENTS (n=50)	PERCENTAGE (100%)
Alive	19	38.0
Dead	31	62.0

FIGURE.23.OUTCOME OF ICH PATIENTS



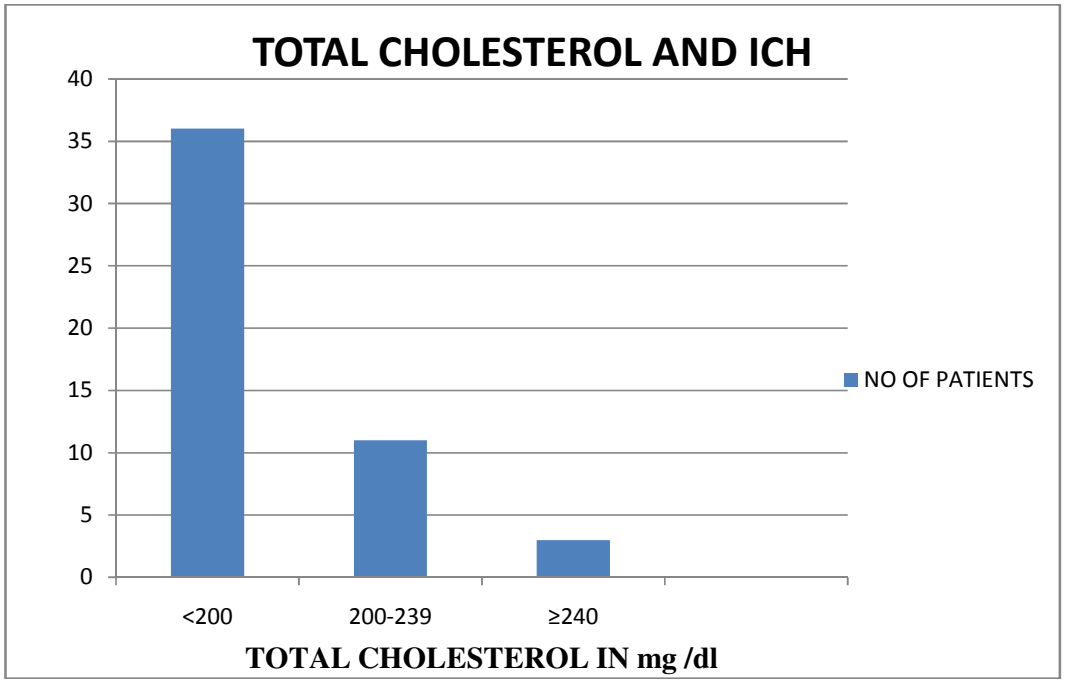
Among our ICH patients about 62% died.

Remaining 38% are alive.

TABLE.14.TOTAL CHOLESTEROL IN PATIENTS

TOTAL CHOLESTEROL (mg/dl)	NO OF PATIENTS (n=50)	PERCENTAGE (100%)
< 200	36	72.0
200 to 239	11	22.0
≥ 240	3	6.0

FIGURE.24.TOTAL CHOLESTEROL IN PATIENTS



A clear majority of patients around 72% in our study group had serum total cholesterol < 200mg/dl.

22% of patients had their serum total cholesterol within range of 200-239 mg/dl.

Only 6 % of patients in our study had their serum cholesterol ≥ 240 mg/dl.

The mean total serum cholesterol of this study group was 168.09±43.74 mg/dl.

To test the statistical significance of this relation we did a t-Test taking 200mg/dl as a normal total cholesterol for normal population.
The study population was partitioned into two groups with this cut off.

TABLE.15.T-TEST FOR TOTAL-CHOLESTEROL

TOTAL-C IN mg/dl	**MEAN**	**S.D**	**STATISTICAL INFERENCE**
< 200 (n=36)	145.9528	**t-TEST** 26.93186	T=-9.915 Df=48 P value= .000<0.05 statistically significant
≥200 (n=14)	225.0000	20.31672	

36 ICH patients in our study had their serum total cholesterol <200mg/dl and their mean total cholesterol was 145.95 mg/dl.

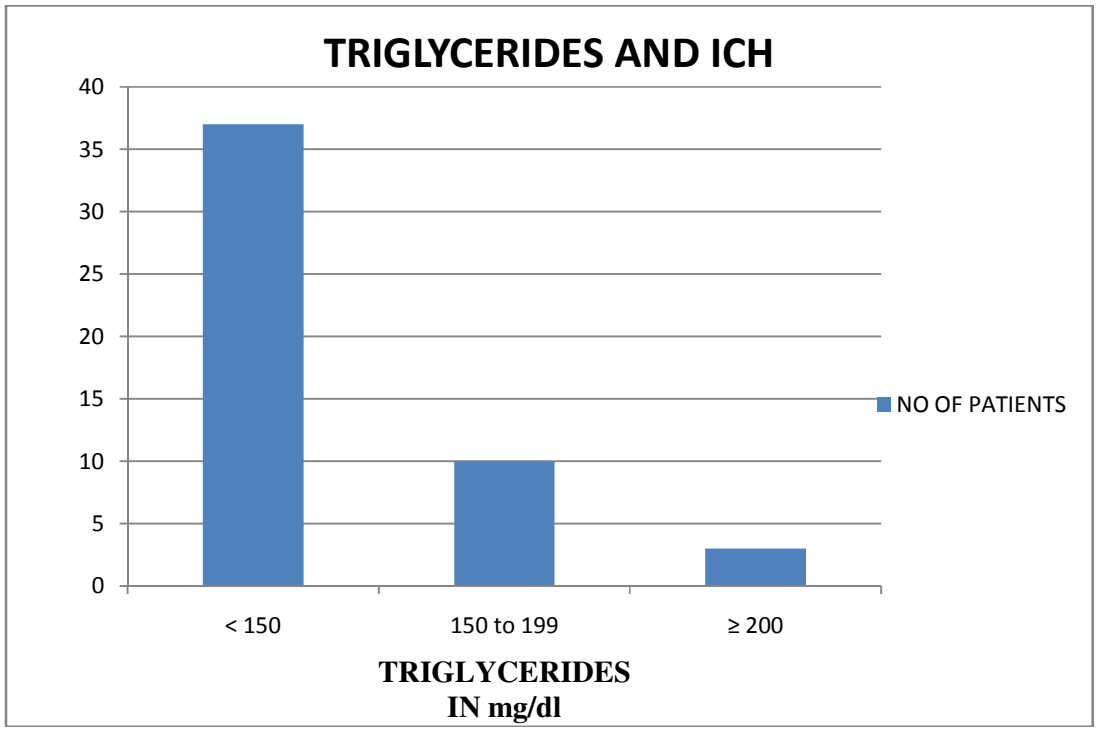
14 ICH patients in our study had their serum total cholesterol ≥200mg/dl and their mean total cholesterol was 225 mg/dl.

Using **t test**, there is statistically significant difference between two means (P value <0.05).

TABLE.16.TRIGLYCERIDES IN PATIENTS

TRIGLYCERIDES IN mg/dl	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
< 150	37	74.0
150 to 199	10	20.0
≥ 200	3	6.0

FIGURE.25.TRIGLYCERIDES IN PATIENTS



74% of patients in this study had their serum triglycerides level <150 mg/dl.

20% of patients had levels from 150-199 mg/dl.

6% of patients had levels ≥ 200 mg/dl.

The mean serum triglyceride among the study population was 124.12±50.76 mg/dl.

To test the statistical significance of this relation we did a t-Test taking 150 mg/dl as a normal triglyceride level for normal population.

The study population was partitioned into two groups with this cut off.

TABLE.17.T-TEST FOR TRIGLYCERIDES

TGL IN mg/dl	**MEAN**	**S.D**	**STATISTICAL INFERENCE**
< 150 (n=37)	100.757	29.009	T=-8.763 Df=48 P value= .000<0.05 Statistically Significant
≥ 150 (n=13)	190.615	39.010	

37 ICH patients in our study had their serum triglyceride < 150 mg/dl and their mean triglyceride was 100.76 mg/dl.

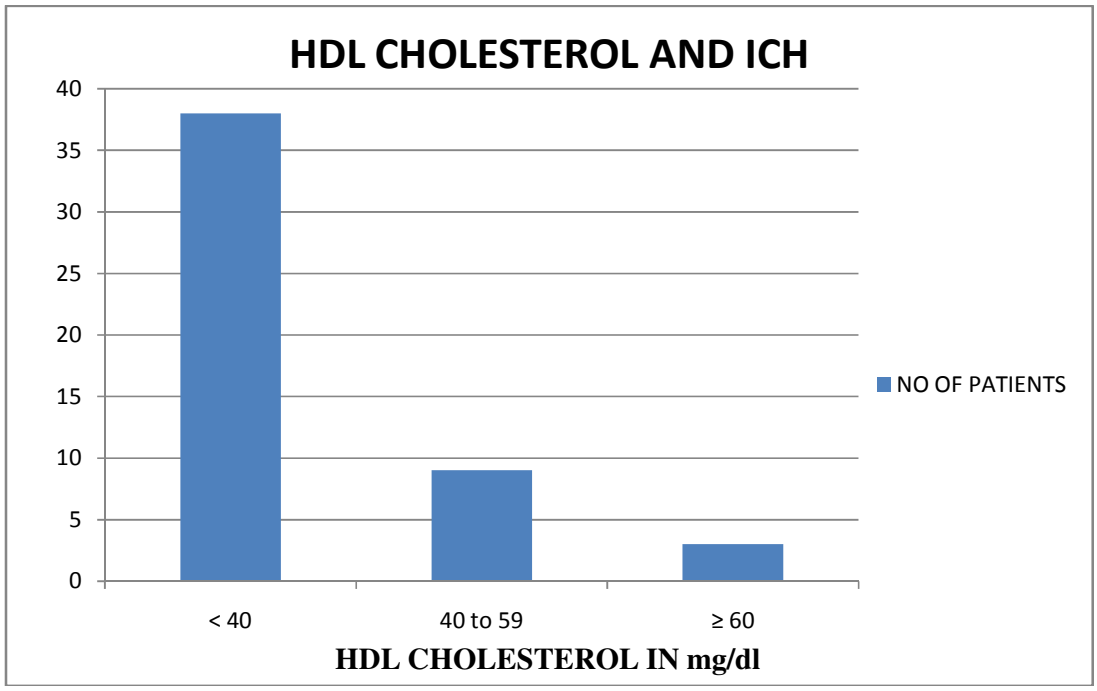
13 ICH patients in our study had their serum triglyceride ≥ 150 mg/dl and their mean triglyceride was 190.62 mg/dl.

Using **t test**, there is statistically significant difference between the two means (P value <0.05).

TABLE.18. HDL CHOLESTEROL IN PATIENTS

HDL CHOLESTEROL IN mg/dl	No.of PATIENTS (n=50)	Percentage (100%)
< 40	38	76.0
40 to 59	9	18.0
≥ 60	3	6.0

FIGURE.26.HDL CHOLESTEROL IN PATIENTS



76% of patients in our study had their serum HDL-C < 40 mg/dl.

18% of patients had levels from 40-59 mg/dl.

6% of patients had levels ≥ 60 mg/dl.

The mean HDL-Cholesterol level in the study population is 32.45± 15.30 mg/dl.

To test the statistical significance of this relation we did a t-Test taking 40 mg/dl as a normal HDL cholesterol for normal population. The study population was partitioned into two groups with this cut off.

TABLE.19.T- TEST FOR HDL CHOLESTEROL

HDL-C IN mg/dl	**MEAN**	**S.D**	**STATISTICAL INFERENCE**
< 40 (n=38)	25.683	**9.007**	T = -9.082 Df = 48 P value=.000<0.05 Statistically Significant
≥ 40 (n=12)	53.883	**10.525**	

38 ICH patients in our study had their serum HDL < 40 mg/dl and their mean HDL was 25.68 mg/dl.

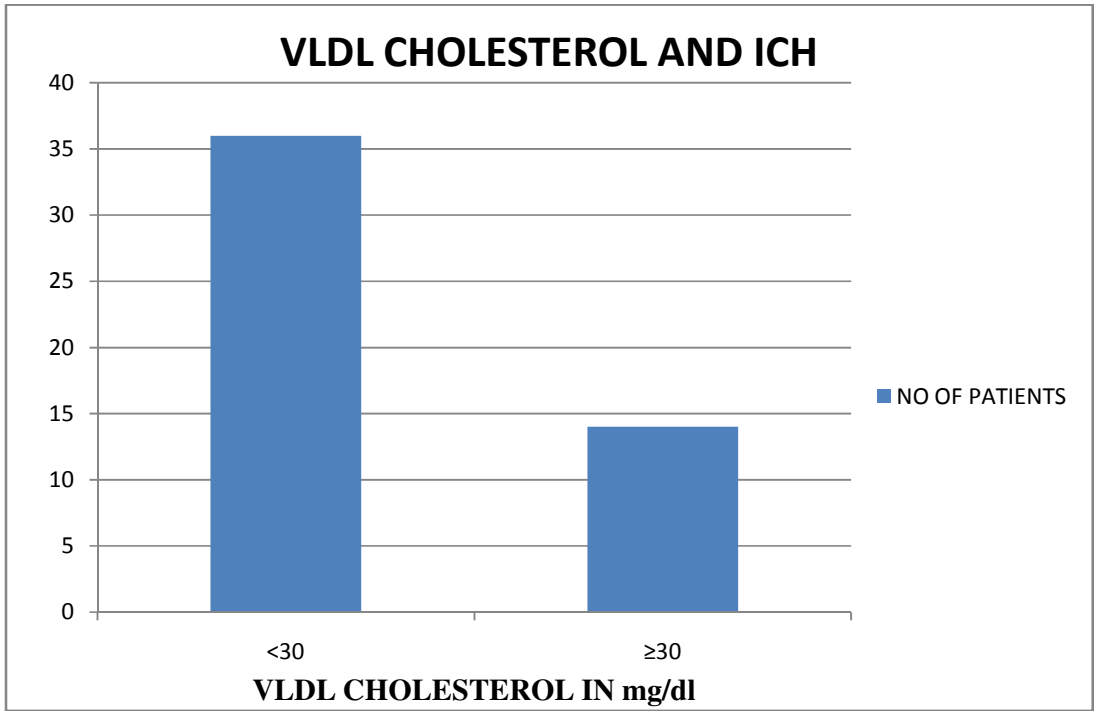
12 ICH patients in our study had their serum HDL ≥ 40 mg/dl and their mean HDL was 53.88 mg/dl.

Using **t test**, there is statistically significant difference between the two means (P value <0.05).

TABLE.20.VLDL CHOLESTEROL IN PATIENTS

VLDL CHOLESTEROL IN mg/dl	NO OF PATIENTS (n=50)	PERCENTAGE (100%)
< 30	36	72.0
≥ 30	14	28.0

FIGURE.27.VLDL CHOLESTEROL IN PATIENTS



72% of ICH patients in our study had VLDL <30mg/dl.

28% of patients had their levels ≥ 30 mg/dl.

The mean VLDL-Cholesterol in our study population was 25.25± 10.14 mg/dl.

To test the statistical significance of this relation we did a t-Test taking 30 mg/dl as a normal VLDL cholesterol for normal population. The study population was partitioned into two groups with this cut off.

TABLE.21.T-TEST FOR VLDL CHOLESTEROL

VLDL-C IN mg/dl	**MEAN**	**S.D**	**STATISTICAL INFERENCE**
< 30 (n=36)	20.408	5.977	T=-8.471 Df=48 P value= .000<0.05 Statistically Significant
≥ 30 (n=14)	37.714	7.650	

36 ICH patients in our study had their serum VLDL < 30 mg/dl and their mean VLDL was 20.41 mg/dl.

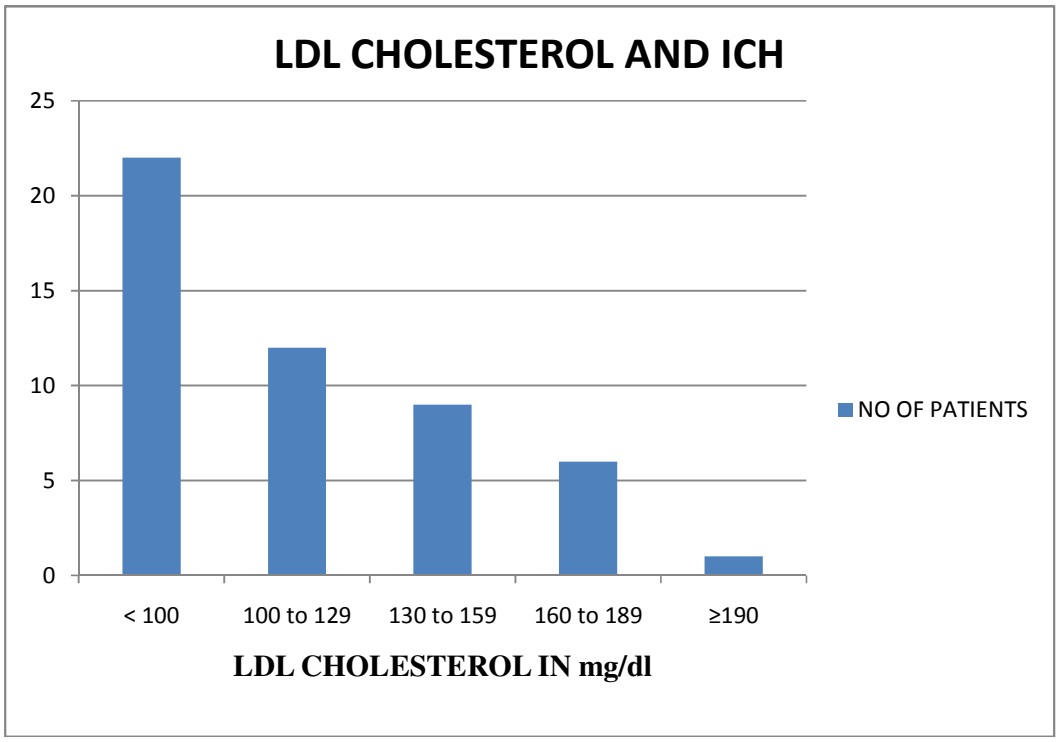
14 ICH patients in our study had their serum VLDL ≥ 30 mg/dl and their mean VLDL was 37.71 mg/dl.

Using **t test**, there is statistically significant difference between the two means (P value <0.05).

TABLE.22. LDL CHOLESTEROL IN PATIENTS

LDL CHOLESTEROL IN mg/dl	NO.OF PATIENTS (N=50)	PERCENTAGE (100%)
< 100	22	44.0
100 to 129	12	24.0
130 to 159	9	18.0
160 to 189	6	12.0
≥190	1	2.0

FIGURE.28.LDL CHOLESTEROL IN PATIENTS



In our study serum LDL-cholesterol was

<100mg /dl in 44 % of the ICH patients,

100-129mg/dl in 24 % of patients,

130-159mg/dl in 18% of patients,

160-189mg/dl in 12% of patients,

≥190 mg/dl in 2 % of patients.

The mean LDL-Cholesterol level in our study population was 108.26± 43.31mg/dl.

To test the statistical significance of this relation we did a t-Test taking 130mg/dl as a normal LDL cholesterol cut off for normal population. The study population was partitioned into two groups with this cut off.

TABLE.23.T-TEST FOR LDL CHOLESTEROL

LDL-C	MEAN	S.D	STATISTICAL INFERENCE
<130 (n=34)	84.6876	26.70511	T=-9.281 Df=48 P value= .000<0.05 Statistically Significant
≥ 130 (n=16)	158.3375	24.97174	

34 ICH patients in our study had their serum LDL cholesterol < 130mg/dl and their mean LDL cholesterol was 84.69 mg/dl.

16 ICH patients in our study had their serum LDL cholesterol ≥ 130mg/dl and their mean LDL cholesterol was 158.34 mg/dl.

Using **t test**, there is statistically significant difference between the two means (P value <0.05).

DISCUSSION

In this study, 50 cases of Intracerebral Haemorrhage (ICH) were included as per the inclusion and exclusion criteria, the observations were recorded and results were compared with other similar studies.

AGE DISTRIBUTION

- The mean age group of ICH patients in our study was 59.1 (± 12.61) years.
- It is in comparison with Iribarren et al[49] where the mean age was 54.2 years and Broderick et al[83] where the mean age was 64.8± 16.1 years.
- Comparing with Indian studies the mean age group was 59.7±14 years in a study from Calicut Ashraf V. Valappil et al[84] and 57.32 ± 12.84 years in a study from AIIMS by Rohit Bhatia et al[85].
- Majority of the patients (48%) belonged to age group of 60-79years in our study. This observation was similar to that in a study from JIPMER Narayan et al[86] where about 46 % of patients were in 60-79 years group.

SEX DISTRIBUTION

- 70% of ICH patients in our study are males;
- 30 % of ICH patients are females in our study.

- The male: female ratio in our study is 2.3: 1.
- This ratio is similar to Ashraf V. Valappil et al[84] with ratio of 2.08:1

and Rohit Bhatia et al[85] where the ratio was 1.9:1.

SITE OF ICH

- Basal ganglia is the common site of ICH in our study contributing to 56% of cases.
- This is in accordance with Thrift et al[87] in which basal ganglia is the most common site of ICH.
- This is also in concordance with Indian studies, Ashraf V. Valappil et al[84] and Narayan et al[86] where basal ganglia was the most common site but the percentages were slightly lower 49% and 45% respectively.

RISK FACTORS AND ICH

SYSTEMIC HT AND ICH

- A clear majority around 80% of ICH patients, are hypertensives in our study. Around 70% of the total ICH patients in our study had Stage II hypertension (BP ≥ 160/100 mmHg).

- Similar trends were seen in Broderick & Brott et al[88] where 73% of ICH patients had systemic hypertension

- In Ashraf V. Valappil et al[84] 76% of ICH patients had hypertension.

DM AND ICH

- Only 34 % of patients in our study had diabetes.

- In a study done in Sweden[89] also around 37% of ICH patients had diabetes. Similar results were seen in Ashraf V. Valappil et al[84] where 38% had diabetes.

ALCOHOL AND ICH

- 58% of patients in our study had history of significant alcohol consumption. Similarly in Quereshi et al[9] alcohol consumption was significant in ICH patients.

- But lesser percent (21%) of ICH patients in Calicut study Ashraf V. Valappil et al[84] had significant alcohol consumption.

SMOKING AND ICH

- Only 48% of patients in our study had history of smoking. It is somewhat lesser compared to western studies Iribarren et al[49] where it was 56.25%. In Indian study Ashraf V. Valappil et al[84], around 36% of patients had history of smoking.

MORTALITY IN ICH

- Among our ICH patients about 62% died.
- The mortality rate in Joseph P. Broderick al[90]., was around 42%.
- In India the motality rate in Shyamal Kumar Das et al[91] was around 48% and in Narayan et al[86] the rate was 50% .

LIPID PROFILE AND ICH

SERUM TOTAL CHOLESTEROL AND ICH

- A clear majority of patients around 72% in our study group, had serum total cholesterol < 200mg/dl.
- Around 54% of our patients had their serum cholesterol values <160mg%.
- The mean total serum cholesterol level of this study group was 168.09± 43.74 mg/dl.

Comparing with international studies,

- MRFIT study[48] showed clear association between low serum cholesterol levels especially below 160mg% with risk of ICH.
- The mean cholesterol levels in ICH patients in MRFIT study was 211.4 ± 43.9 mg/dl.

- The Honolulu Heart Program Yano et al[92] showed increased risk of ICH in those with serum cholesterol <189 mg%.

- In Konishi et al[93] the mean serum total cholesterol in ICH patients was 164± 2mg%.

Comparing with Indian studies,

- In the Calicut study Ashraf V. Valappil et al[84] , 43% of ICH patients had serum cholesterol < 160mg%.

- The mean serum total cholesterol in this study was 177 ± 39 mg%.

TGL AND ICH

- 74% of patients in this study had their serum triglycerides level < 150 mg/dl.

- The mean serum triglyceride among our study population was 124.12± 50.76 mg/dl.

- This is in concordance with Sturgeon et al[94] where 81.48% of ICH patients had their serum triglyceride concentration <158mg%.

- There is in discordance with Ashraf V. Valappil et al[84] where mean triglyceride concentration in was 84 ± 35.5 mg%.

HDL-C AND ICH

- 76% of patients in our study had their serum HDL-C <40 mg/dl.
- The mean HDL-Cholesterol level in the study population is 32.45 ± 15.30 mg/dl.
- The mean HDL-C in Ashraf V. Valappil et al[84] was 42± 12mg%

LDL-C AND ICH

- In our study the serum LDL-cholesterol was <130mg /dl in 68 % of the ICH patients.
- The mean LDL-Cholesterol level in our study population was 108.26± 43.31mg/dl.
- Comparing with Hiroyuki et al[95] 59.84% of ICH patients had LDL-C less than120mg%
- In Calicut study Ashraf V. Valappil et al[84] the mean LDL-C was 114± 37mg%.

VLDL-C AND ICH

- 72% of ICH patients in our study had VLDL <30mg/dl.
- The mean VLDL-Cholesterol in our study population was 25.25± 10.14 mg/dl.

STRENGTHS AND LIMITATIONS OF THE STUDY

- This study has included patients with intracerebral haemorrhage excluding the secondary causes of ICH.
- Though many foreign studies and some Indian studies have been conducted in studying lipid profile in ICH, only few studies are available in south India especially Tamilnadu. Our study involves study of lipid profile in a group of 50 ICH patients in and around Thanjavur generating insights into the characteristics of the disease in Tamilnadu and its correlation with serum lipid levels.
- The limitation of our study is that the dietary habits and physical activities of patients could not be explored.
- This study is based on a single center and hospital based, hence the results obtained may not reveal the true burden of the disease in the community taken as a whole.

SUMMARY

1. Majority of the patients of intracerebral haemorrhage in our study were > 55 years.
2. Majority of the ICH patients in our study were males around 70%.
3. Basal ganglia was the most common site of ICH.
4. Hypertension was the most significant risk factor in our study. This reinforces the fact that it is most important to control the elevated blood pressure in the community which has strong association with incidence of ICH.
5. The total serum cholesterol concentration was low < 200mg/dl in 72 % of our patients.
6. The mean serum cholesterol was 168.09 ± 43.74 mg%.
7. The serum triglycerides level was <150 mg/dl in 74% of patients in this study, with a mean of 124.12 ± 50.76 mg%.
8. The HDL-C was < 40 mg/dl in 76% of patients in our study.
9. The VLDL-C was < 30mg/dl in 72% of ICH patients in our study.

CONCLUSION

- Majority of intracerebral haemorrhage patients in our study had lower levels of total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein and very low density lipoprotein.
- The following mechanism is proposed for inverse association of serum lipids and ICH. Cholesterol and triglycerides form an integral part of cell membrane of vascular endothelium and erythrocytes. When their levels are low, weakening of endothelium and increased erythrocyte fragility occurs, more significantly in the presence of hypertension which predispose to micro aneurysms and later on ICH.
- Whether the inverse association of serum cholesterol and ICH is a true causal association or only by chance due to some other common confounding factor needs to be evaluated with large scale studies.
- The public health impact of this inverse correlation of serum cholesterol and ICH has to be interpreted cautiously considering the baseline characteristics of the population. Aggressive methods of decreasing cholesterol levels to very low values should not be followed as a routine practice. Further studies with larger sample size concentrating on the pathophysiological effects of serum lipids and ICH are very much essential.

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CONSENT FORM

I _____ hereby give consent to participate in the study conducted by **DR DEEPIKA.S,** Post graduate in the Department of General Medicine ,Thanjavur Medical College & Hospital, Thanjavur – 613004 and to use my personal clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations

Place :

Date : Signature of participant

STUDY OF LIPID PROFILE IN INTRACEREBRAL HAEMORRHAGE

PROFORMA

NAME: D.O.A:

AGE: SEX: MALE/FEMALE D.O.D:

OCCUPATION: ADDRESS:

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

1. Weakness of limbs:

Right upper limb: left upper limb:

Right lower limb: left lower limb:

Duration: Onset: sudden / insidious

2. Loss of consciousness: YES/NO DURATION:

3. CONVULSIONS:

a) DURATION:

b) NO. OF EPISODES:

c) TYPE OF CONVULSION: PARTIAL / GENERALISED

4. OTHER ASSOCIATED COMPLAINTS:

a. FEVER:

b. HEADACHE:

c. NAUSEA/ VOMITING:

d. OTHERS:

PAST HISTORY:

- H/O STROKE / INFECTIONS / TRAUMA
- H/O SHT / DM / TB /CKD/CAHD/BLEEDING DISORDER
- H/O DRUG INTAKE

FAMILY HISTORY:

- ANY SIMILAR COMPLAINTS IN OTHER FAMILY MEMBERS
- COMORBID ILLNESS: YES / NO
- FAMILY HISTORY OF OBESITY:

PERSONAL HISTORY:

- HABITS-
  - SMOKING: YES/ NO. IF YES, DURATION:
  - ALCOHOL: YES/ NO. IF YES, DURATION:

- TOBACCO CHEWING: YES/ NO
- DRUG ABUSE: YES/ NO. IF YES, DRUG:
- EXPOSURE TO STDs: YES/ NO

- DIET:

EXAMINATION OF THE PATIENT

GENERAL EXAMINATION:

- BUILD AND NOURISHMENT:
- PALLOR / ICTERUS/ CLUBBING / CYANOSIS/ PEDAL EDEMA / LYMPHADENOPATHY
- MARKERS OF HYPERLIPIDEMIA:
- ANY NEUROCUTANEOUS MARKERS:

VITAL SIGNS:

PULSE: RR:

BP: TEMP:

CENTRAL NERVOUS SYSTEM EXAMINATION:

A) HIGHER MENTAL FUNCTIONS

a. CONSCIOUSNESS:
b. ORIENTATION TO : TIME/ PLACE / PERSON
c. APPEARANCE AND BEHAVIOUR:

d. ATTENTION:

e. VIGILANCE:

f. LANGUAGE:

g. MEMORY

h. INTELLIGENCE

B) CRANIAL NERVES RT

LT

1) SENSE OF SMELL

2) ACUITY OF VISION

FIELD OF VISION:

COLOUR VISION:

FUNDUS:

PTOSIS: PRESENT / ABSENT

PUPILS- SIZE, SHAPE: REFLEXES: DIRECT / INDIRECT

3.4.6 .EXTRAOCULAR MOVEMENTS:

5. MOTOR:

SENSORY:

REFLEXES: CORNEAL / CONJUCTIVAL/JAW JERK

7. MOTOR:

TASTE – ANT 2/3 rd TONGUE:

8. RINNE'S

WEBER'S:

9. TASTE –POST 1/3rd TONGUE, PALATE

10. PALATAL MOVEMENT:

GAG REFLEX:

PHONATION:

SWALLOWING:

11 .STERNOCLEIDOMASTOID:

TRAPIZEUS:

12. TONGUE MOVEMENTS:

WASTING AND FASCICULATIONS:

C) MOTOR SYSTEM: **RT** **LT**

NUTRITION

TONE

POWER

SHOULDER

ELBOW

WRIST

HAND GRIP

HIP

KNEE

ANKLE

REFLEXES:

SUPERFICICAL - CORNEAL

CONJUNCTIVAL

PLANTAR

CREMASTRIC

ABDOMINAL

DEEP - JAW JERK

BICEPS

TRICEPS

SUPINATOR

KNEE

ANKLE

COORDINATION

UPPER LIMB- FINGER NOSE TEST

FINGER NOSE FINGER TEST

LOWER LIMB- HEEL KNEE TEST

TANDEM WALKING

ABNORMAL MOVEMENTS:

D) SENSORY SYSTEM:

TOUCH

PAIN

TEMPERATURE

VIBRATION

JOINT POSITION SENSE

STEREOGNOSIS

TACTILE LOCALISATION

TWO POINT DISCRIMINATION

ROMBERG'S SIGN

E) CEREBELLAR SIGNS:

F) GAIT:

G) SIGNS OF MENINGEAL IRRITATION:

H) SKULL AND SPINE:

OTHER SYSTEMS:

CARDIOVASCULAR SYSTEM:

RESPIRATORY SYSTEM:

PER ADBOMINAL EXAMINATION:

INVESTIGATIONS:

1) URINE

ALBUMIN

SUGAR

DEPOSITS

2) BLOOD SUGAR:

3) BLOOD UREA: 4) SERUM CREATININE:

4) BT : CT:

5) PT: aPTT :

6) SERUM ELECTROLYTES:

   a. SODIUM

   b. POTASSIUM

7) LIPID PROFILE

   a. TOTAL CHOLESTEROL:

   b.TRIGLYCERIDES

   c. LOW DENSITY LIPOPROTEIN:

   d.HIGH DENSITY LIPOPROTEIN

   e. VERY LOW DENSITY LIPOPROTEIN

8) COMPLETE HAEMOGRAM

   a. Hb %:

   b. TC:

   c. DC:

   d. RBC:

   e. PLATELETS:

   f. PCV:

   g. ESR:

   h. PS

9) VCTC:

10) ECG:

11) ECHO:

12) CHEST XRAY:

13) CT BRAIN:

14) MRI BRAIN/MRA /MRV:

15) CAROTID DOPPLER STUDY:

16) USG ABDOMEN:

17) OTHERS:

MASTER CHART

S.NO	IP NO	NAME	AGE	SEX	SITE OF ICH	SHT	BP STAGE	DM	ALCOHOL	SMOKING	OUTCOME
1	76	KUMARASAMY	70	M	L BASAL GANGLION	NO	Below 140/90	NO	YES	NO	ALIVE
2	163	RAMASAMY	50	M	R PARIETO OCCIPITAL	YES	Above 160/100	NO	YES	YES	DEAD
3	819	MARIAMMAL	60	F	L BASALGANGLIA	NO	Below 140/90	YES	NO	NO	ALIVE
4	843	VEERA	40	M	L THALAMIC	NO	Below 140/90	NO	YES	YES	DEAD
5	1131	KANNAN	54	M	R BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
6	1151	MALAIMANNAN	32	M	R BASALGANGLIA	YES	Above 160/100	YES	YES	YES	DEAD
7	1316	LAKSHMI	70	F	L BASALGANGLIA	NO	Below 140/90	NO	NO	NO	ALIVE
8	1337	CHINNAMMA	59	F	L TEMPORAL	YES	Above 160/100	NO	NO	NO	ALIVE
9	1396	MUTHUSAMY	60	M	L BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
10	2029	BALUSAMY	87	M	R PARIETOTEMPORAL	YES	Above 160/100	NO	YES	NO	ALIVE
11	3001	JALAPATHI	57	M	R THALAMIC	YES	Above 160/100	YES	YES	YES	DEAD
12	3338	RAMALINGAM	50	M	L BASAL GANGLION	NO	Below 140/90	NO	YES	YES	ALIVE
13	3390	SUBASH	63	M	R BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
14	4721	GOWRI	45	F	R BASALGANGLIA	YES	Above 160/100	NO	NO	NO	DEAD
15	5341	JEGANANTHAN	78	M	L BASALGANGLIA	YES	Above 160/100	YES	YES	YES	DEAD
16	5972	VEDHASORUBINI	58	F	L BASALGANGLIA	YES	Above 160/100	YES	NO	NO	DEAD
17	6926	RAVI	50	M	B/L PONS AND MIBRAIN	YES	Above 160/100	YES	NO	NO	DEAD
18	9826	EDWARD	55	M	R OCCIPITAL	YES	Above 160/100	YES	YES	YES	DEAD
19	9970	XAVIER	65	M	L BASALGANGLIA	YES	Above 160/100	NO	NO	YES	DEAD
20	11405	MARIAPPAN	60	M	L BASALGANGLIA	NO	Below 140/90	NO	YES	NO	DEAD

S.NO	IP NO	TOT CHOL	TGL	HDL-CHOL	VLDL CHOL	LDL-CHOL
1	76	99.6	157	11.5	31.4	56.7
2	163	119	120	21.4	24	73.6
3	819	205	90	24.4	18	162.6
4	843	124	96	25.8	19.2	79
5	1131	124	172	14	34.4	75.6
6	1151	145	184	30	36.8	78.2
7	1316	165	60.2	28.7	12.04	102.7
8	1337	238	81	34.8	16.2	187
9	1396	147	128	11.7	25.6	109.7
10	2029	149	83	46	16	95
11	3001	142	187	8.56	37.4	96.04
12	3338	157	107	28	28	108.8
13	3390	118	141	25	28.2	64.8
14	4721	183	69	39	13.8	130.2
15	5341	99.8	131	30.2	26.2	43.4
16	5972	150	144	30	28.8	91.2
17	6926	195	64.8	55	12.96	127.04
18	9826	124	172	11	34.4	78.6
19	9970	204	201	31	40.2	132.8
20	11405	190	73	41.9	14.6	133.5

S.NO	IP NO	NAME	AGE	SEX	SITE OF ICH	SHT	BP STAGE	DM	ALCOHOL	SMOKING	OUTCOME
21	11755	KARUPAIYA	50	M	L PARIETOOCCIPITAL	YES	Above 160/100	NO	YES	YES	DEAD
22	12332	RAMALINGAM	60	M	R BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
23	18000	KAMARAJ	45	M	R BASALGANGLIA	YES	Above 160/100	YES	YES	YES	DEAD
24	18554	VIJAYAGURU	30	M	R BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
25	21716	MARI	60	M	L BASALGANGLIA	YES	Above 160/100	NO	YES	YES	ALIVE
26	24054	SIVAKUMAR	69	M	R TEMPORAL	YES	140/90 to 159/99	NO	YES	NO	ALIVE
27	24709	JOSEPH	78	M	R CEREBELLUM	YES	Above 160/100	NO	YES	YES	ALIVE
28	33261	VELLADURAI	65	M	L BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
29	35120	ASHA	66	F	R BASALGANGLIA	NO	Below 140/90	YES	NO	NO	DEAD
30	35153	NATARAJ	55	M	R BASALGANGLIA	YES	Above 160/100	NO	YES	YES	DEAD
31	40224	CHINNATHAMBI	74	M	L TEMPORAL	YES	Above 160/100	NO	YES	NO	DEAD
32	42205	RAMAN	60	M	R THALAMIC	YES	140/90 to 159/99	NO	NO	NO	ALIVE
33	42223	SEKAR	40	M	R CEREBELLUM	YES	Above 160/100	NO	YES	NO	DEAD
34	42288	CHINNAPONNU	40	F	L THALAMIC	YES	Above 160/100	YES	NO	NO	DEAD
35	42344	REVATHY	67	F	L CEREBELLUM	YES	Above 160/100	NO	NO	NO	DEAD
36	42335	CLARA	64	F	R TEMPORAL	NO	Below 140/90	YES	NO	NO	ALIVE
37	42362	RAVI	55	M	R BASALGANGLIA	YES	Above 160/100	NO	YES	NO	ALIVE
38	52444	MALLIKADEVI	60	F	L BASALGANGLIA	YES	Above 160/100	YES	NO	NO	DEAD
39	59955	KALIAMMAL	63	F	L BASALGANGLIA	YES	Above 160/100	YES	NO	NO	DEAD
40	66551	SUSILA	82	F	R BASALGANGLIA	YES	140/90 to 159/99	NO	NO	NO	ALIVE
41	72317	DHARMALINGAM	45	M	R BASAL GANGLION	YES	140/90 to 159/99	NO	NO	NO	ALIVE

S.NO	IP NO	TOT CHOL	TGL	HDL-CHOL	VLDL CHOL	LDL-CHOL
21	11755	201	123	32	24.6	144.4
22	12332	171	119	66.9	23.8	23.8
23	18000	145	197	10	39.4	66.2
24	18554	100.8	72.3	29.9	14.5	56.4
25	21716	250	143	38.9	28.6	182.5
26	24054	252	302	50	60.4	141.6
27	24709	210	62	31.5	12.4	166.1
28	33261	153	184	21.3	36.8	94.9
29	35120	211	150	35	30	146
30	35153	220	160	37	32	151
31	40224	116	83	67	32.4	16.6
32	42205	157	68.8	42.4	13.8	100.8
33	42223	218	59	36.4	11.8	169.8
34	42288	189	115	32.8	23	133.2
35	42344	143	72	25	14.4	103.6
36	42335	217	125	73	25	119
37	42362	228	133	25.7	26.6	175.7
38	52444	228	135	46	27	155
39	59955	172	98	45.5	19.6	106.9
40	66551	150.5	102	33	20.4	97.1
41	72317	137	140	17.5	28	91.5

S.NO	IP NO	NAME	AGE	SEX	SITE OF ICH	SHT	BP STAGE	DM	ALCOHOL	SMOKING	OUTCOME
42	77177	MARIYAMMAL	82	F	L PARIETO OCCPITAL	YES	Above 160/100	YES	NO	NO	DEAD
43	82335	SEKAR	45	M	L BASALGANGLIA	YES	Above 160/100	NO	YES	YES	ALIVE
44	82965	RAMAIYAH	60	M	R THALAMIC	YES	Above 160/100	NO	NO	YES	DEAD
45	83706	BAKYANATHAN	60	M	L TEMPORAL	YES	140/90 to 159/99	NO	NO	NO	ALIVE
46	89738	VENKATESH	80	M	L THALAMIC	YES	Above 160/100	YES	YES	YES	DEAD
47	91220	SELVAKANTHAN	68	M	L BASAL GANGLION	YES	Above 160/100	NO	YES	YES	ALIVE
48	91284	UMMASALIMA	60	F	L THALAMUS	YES	Above 160/100	YES	NO	NO	DEAD
49	91334	SAROJA	53	F	L TEMPORAL	NO	Below 140/90	NO	NO	NO	ALIVE
50	91996	KANNAN	56	M	L BASAL GANGLION	NO	Below 140/90	YES	YES	YES	ALIVE

S.NO	IP NO	TOT CHOL	TGL	HDL-CHOL	VLDL CHOL	LDL-CHOL
42	77177	160	187	58.9	37.4	63.7
43	82335	268	80.9	29.8	16.2	222
44	82965	144	45	30	9	106
45	83706	83.6	116	18.5	23.2	41.9
46	89738	159	131	20.6	26.2	112.2
47	91220	162	112	38	22	87
48	91284	175	80	54	16	105
49	91334	146	125	12	25	109
50	91996	159	225	16	45	97.4

KEY TO MASTER CHART

IP NO – IN PATIENT NUMBER

M-MALE

F-FEMALE

L-LEFT

R-RIGHT

B/L- BILATERAL

SHT-SYSTEMIC HYPERTENSION

BP-BLOOD PRESSURE

DM-DIABETES MELLITUS

TOT-CHOL-TOTAL CHOLESTEROL IN MG/DL

TGL-TRIGLYCERIDE IN MG/DL

HDL-CHOL-HIGH DENSITY CHOLESTEROL IN MG/DL

VLDL-CHOL-VERY LOW DENSITY CHOLESTEROL IN MG/DL

LDL-CHOL-LOW DENSITY CHOLESTEROL IN MG/DL